RECENT ADVANCES IN CARDIOLOGY

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BY

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PREFACE TO THE FIFTH EDITION

It was rather over thirty years ago that we first contemplated, with some diffidence, a review of the advances that had been made in the then young and hardly formed subject of Cardiology. What then was an "advance" and what was "recent" chiefly occupied our thoughts To-day the vast flood of publications makes the question of recentness answer itself, while time soon shows what constitutes an "advance." It is not easy to keep abreast with this subject nowadays in all its many complicated and technical ramifications. The [illegible]

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ment of other subjects on a larger scale, for it is now necessary to focus on certain selected matters where new knowledge has aroused special interest, rather than to try to review the subject as a whole Of course, after ten years it has been necessary to write the book completely afresh and to include a number of new illustrations.

In preparing this edition we have had the advantage of being able to enlist the valuable help of Dr Wallace Brigden of the Cardiac Department of the London Hospital and of the National Heart Hospital His responsibility extends to the writing of Chapters 2, 3 and 5 and the section on syncope The rest of the book is the combined responsibility of the original authors—for the last time.

The very up-to date reviewer must remember, as we have pointed out before, that the time of literary gestation tends to increase so that many months must elapse between conception on paper and parturition in print

In recent years the cardiac catheter has added enormously to our knowledge in the field of hæmodynamics, although in much it is becoming a question of confirming what has already been shrewdly suspected Congenital defects are an ever-growing interest. The detailed surgical treatment is a technical matter outside the scope of this book. At the present moment all depends on giving the surgeon enough time in a bloodless field, then with the help of modern anæsthesia he will be able to do almost anything The

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new pathological knowledge The riddle of hypertension is still unsolved, but its effects are better understood and to some degree better mitigated. Disease of the coronary arteries is still obscure; more knowledge of its biochemistry will be the next step, but there is a long way to go. Heart failure is better understood in many aspects, and the knowledge of the causation and treatment of œdema has advanced a good deal.

As in former editions we have aimed at presenting in a practical way new knowledge; remembering, as always, that the academic of to-day is often the commonplace of tomorrow Complicated techniques become simple once the secrets they reveal have been learned, so that it becomes easy to blend their information into the stock of common knowledge, when this is founded on the basic principles of physiology. Thirty years ago one stressed the importance of the myocardium as taught by Mackenzie. Now one goes back to Harvey and stresses the hæmodynamics of the circulation of the blood!

We wish, once again, to thank our publishers, always patient, helpful and hopeful, over many years

T. E — C. W C B

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ACKNOWLEDGEMENTS

ALTHOUGH most of the illustrations have been prepared from personal and hospital records of patients who have been under their care, the authors wish to express their appreciation of the ready co-operation they have received in connection with these and others appearing in this edition to—

Dr. M Godfrey and the Editor of *King's College Hospital Gazette* for permission to reproduce Figs. 11 and 12; to Dr. William Evans for Figs 57 and 58; to Dr J. P D. Mounsey for Fig. 43; to the Editor of the *British Heart Journal* for Figs. 31, 34, and 38 and the Editor of the *Lancet* for Figs. 28, 46, 47, 49 and 52–56 taken from articles by Dr. Wallace Brigden Figs. 107 and 114 also from the *British Heart Journal* and Figs. 99 and 100 from the *Lancet* come from articles written by one of us (C.W.C.B.), and have appeared in earlier editions

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CHAPTER 1

CONGENITAL CARDIAC DEFECTS

It is not possible to classify these complex and often multiple defects satisfactorily. Various attempts have been made on a

is not of much use nowadays The relative volumes of the systemic and pulmonary flow has also been suggested, but these may vary too, also the volumes of the shunts The best basis is anatomical or embryological Here the difficulty arises that sometimes there are multiple defects Many of these cases cannot survive, and are not of much clinical interest. Furthermore the reason of the derangement in development is usually obscure Nevertheless, from the practical point of view of accurate diagnosis, which may offer some chance of surgical treatment, and also of prognosis, the anatomical basis seems best, and with the help of modern methods any case that seems likely to survive at all can usually be diagnosed accurately.

The contents of this chapter must be set forth in some sort of order The following arrangement, based partly on anatomical, partly on physiological and partly on embryological features of these diverse and disconnected topics, is given for what it is worth.

ARRANGEMENT

1. Anomalies of Septal Formation. CARDIAC.

(a) *Cyanotic*
Cor biloculare Cor triloculare biatriatum Cor triatriatum
Cor triloculare biventriculare

(b) *Potentially cyanotic* With pulmonary plethora.
Atrial septal defect
Ventricular septal defect Eisenmenger Complex.

2. Anomalies of Septal Formation. AORTIC

(a) *Cyanotic* With normal or reduced pulmonary flow.
Persistent truncus arteriosus.

(*b*) *Acyanotic.* With pulmonary plethora.
Aortico-pulmonary communication.
(Aneurysm of sinus of Valsalva: may be no shunt)

3. Anomalies associated with torsion of the Truncus Arteriosus and absorption of the Bulbus Cordis.

(*a*) *Cyanotic.*
1. Transposition of great vessels. With pulmonary plethora.
2. Tetralogy of Fallot. Ventricular septal defect. With pulmonary oligæmia.
3. Eisenmenger Complex. Ventricular septal defect. With pulmonary plethora.

(*b*) *Acyanotic or late cyanotic.*
Infundibular pulmonary stenosis with pulmonary oligæmia

(*c*) *Acyanotic*
Subaortic stenosis.

4. Valvular Anomalies.

(*a*) *Cyanotic*
Ebstein's deformity: with pulmonary oligæmia
Tricuspid atresia: with pulmonary oligæmia

(*b*) *Acyanotic or late cyanotic.*
Pulmonary stenosis (simple) and A.S D. (often)

(*c*) *Acyanotic.*
Aortic stenosis
Anomalies of aortic and pulmonary valves.

5. Anomalies of the development of the Aortic Arches.

Persistent right aortic arch. double aortic arch
Coarctation of the aorta.
Anomalies of main branches.
Patent ductus arteriosus.
Anomalies of the coronary arteries

6. Dextrocardia.

7. Miscellaneous.

Pulmonary arteriovenous fistulæ
Anomalies of the pulmonary artery and its branches.
Congenital heart block.
Endocardial fibroelastosis.
Anomalies of great veins and pulmonary veins.

DEVELOPMENT OF THE HUMAN HEART

Although *no recent advance is a feature here, some account of* this complex process should help in understanding the nature and origin of the defects in its achievement.

During its development the mammalian heart passes through various stages which resemble the hearts of lower animals; in each individual the history of the development in various species is recapitulated. The congenital malformations of the human heart recall structures found in the hearts of fishes, amphibians, reptiles and birds

The process of development aims at establishing a pulmonary circulation "in parallel" with the systemic, instead of "in series." But they must communicate with each other, so the two are also "crossed" The heart begins as a fusion of two straight tubes placed on either side of the body, which are brought together as the primitive ventral cleft closes in In the 3 mm. embryo this simple tube is already becoming divided into four chambers, the sinus venosus at the tail end, the auricle, the ventricle, and the bulbus cordis at the head end This stage represents the heart of some fishes As the primitive cardiac tube increases in length, between two fixed points, it becomes kinked or bent, or twisted upon itself (Fig 1) The ventricle grows downwards and forwards, the auricle upwards and backwards The ventricular part becomes a loop bent on itself in a v-shaped manner, forming in the angle of the loop the bulbo-ventricular groove A twist also develops, clockwise at the ventricular end, anti-clockwise at the venous end (Fig 2)

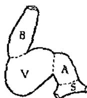


FIG 1

A Auricle
B Bulbus Cordis
S. Sinus Venosus.
V Ventricle

(After Pichon)

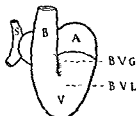


FIG 2

A Auricle.
B Bulbus Cordis
B V G Bulbo-ventricular groove.
B V L Bulbo-ventricular loop
S. Sinus Venosus
V. Ventricle

(After Pichon)

Division of truncus and bulbus. In order to develop the two circulations in parallel, the truncus arteriosus must be divided. A septum forms across the truncus from two lateral ridges. At the distal end of the truncus, furthest from the heart, the plane in which they lie is at right angles to the antero-posterior plane of the body (Fig. 3). According to the theory of Spitzer (1929) two processes of torsion take place. In the first torsion, while the upper or distal part of the tube is turned through 180° in an *anti-clockwise* direction,

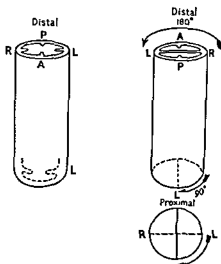




FIG. 3 FIG 4

the lower or proximal end is twisted through 90° in a *clockwise* direction (Fig. 4). The lower end of the septum will now be across, at right angles, in the antero-posterior plane. According to Lev and Saphir (1937) a second torsion takes place about the sixth week of fœtal life This is in fact a "detorsion," for the distal end twists back in a *clockwise* manner 150°, and the proximal end twists back 45° in an *anti-clockwise* direction, towards the left The incomplete interventricular septum is lying at an angle of 45° to the left of the antero-posterior plane (the right ventricle being somewhat to the right and in front) The bulbar septum can now join the interventricular septum and the partition is finally completed by the upper membranous portion.

This detorsion at the end of the tube proximal to the heart determines the relative positions of the pulmonary artery and

aorta, the pulmonary artery arising rather in front and to the right and running upwards to the left and backwards; while the aorta comes from the left, forwards upwards and to the right. The two circulations are now "crossed" as well as "in parallel."

It can now be seen that if the "detorsion" is carried too far the aorta will be moved too far to the right, over the septum or even completely dextroposed over the right ventricle—while the pulmonary artery, if not small and deformed as in the Tetralogy of

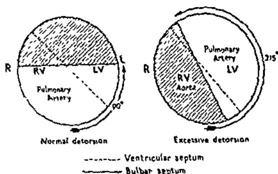


FIG. 5

Fallot, may arise wholly from the left ventricle (complete transposition) (Fig 5)

The septum of the truncus, called the aortico-pulmonary septum, becomes continuous with that end of the bulbar septum, which is distal or furthest from the heart. The distal part of the bulbar septum fuses with the proximal part of the bulbar septum The two sides, right and left, with their efferent trunks, are thus divided by a partition

The critical period of development lies within the fifth and eighth weeks [illegible] form [illegible] take [illegible] bulb [illegible] many defects arise from the imperfect completion of these changes, and for this reason the defects are finally often multiple

Abnormal rotation of the bulbus and truncus will result in a faulty position (transposition) of the aorta and pulmonary artery. A primitive single truncus may persist owing to the failure of the septum to develop Dextroposition of the aorta may result from

this transposition, varying in degree according to the amount of excess *detorsion above the 45° anti-clockwise* movement needed to bring the bulbar and ventricular septa into line.

The absorption of the bulbus cordis. The bulbus persists in fishes as a separate chamber between the ventricle and the aorta In the human heart the part embedded in the bulbo-ventricular groove, which forms the bulbo-ventricular ridge, ultimately disappears. It is at this spot that the 45° of detorsion or untwisting of the cardiac end of the bulbus occurs. This spot is called the bulbo-ventricular loop (Fig 2). The correct detorsion and embedding is very important. If the twist is excessive, then the absorption of the bulbus goes wrong. Most of the bulbus is absorbed into the right ventricle to form ultimately its conus arteriosus or infundibulum. If this process is imperfect, stenosis and hypoplasia of the infundibular part of the conus and of the pulmonary artery result, as Keith supposed In the Tetralogy there is some degree of transposition or dextroposition of the aorta, and this anomaly lies behind two other features—the deformed pulmonary orifice and the patent septum A small part of the bulbus is absorbed into the left ventricle just below the aortic valves Incomplete absorption here causes sub-aortic stenosis

The atrial canal. Between the primitive atrium and ventricle lies the atrial canal This is divided into two channels by the fusion of two endocardial swellings, which lie one in front and one behind, to form a partition The musculature of the atria and ventricles, hitherto continuous, is divided by an ingrowth of connective tissue, so that only a few strands are left, which later become the bundle of His This may be interrupted in congenital heart block The septa of the atria and ventricles fuse with these endocardial swellings If they fail to develop, defects in the septa and atrio-ventricular valves result.

Ætiology. Practically nothing has been known about the causation of congenital cardiac defects They are often associated with abnormalities elsewhere Fœtal endocarditis has had but little attention in recent years The important evidence that rubella may play a part has revived interest in some such possibility The incidence of congenital defects of various sorts, of which 57% were cardiac, in children whose mothers had rubella in early pregnancy, is very suspicious of some association Investigation along these lines, *with more information as to the type of defect may be* valuable Other virus infections may need consideration

There is a very slight familial incidence A woman who has had

one child with a congenital defect of the heart is rather more likely to have another than a woman who has had normal children.

ELECTROCARDIOGRAPHY

General features. The enlargement of one or more chambers of the heart may be indicated. Difficulties concern the right side The bipolar leads, which are often biphasic, show deviation of the electrical axis in some cases This should be over + 120° in hypertrophy It must be remembered that in the first few months of life the right ventricle ... This determines ... is of high voltage ... end of the first year the S wave is much larger; Rs tends to become rS A Q wave seen in V1 at this time indicates pathological enlargement of the right ventricle (1). The slightly delayed intrinsicoid deflection to 0 04 sec, bundle branch block being absent, is a point. The R/S or R/Q ratio in VR is over 1 0. The R/S ratio in V1 falls from 7 0 in the first three months to 2 5 at a year, while the ratio of R/S in V5 rises from 0 5 in the first three months to 0 8 at the end of 12 months There is some overlap in V1 in the very young, but in V5 the large S wave is distinctive (4)

The T wave is normally negative from V1 to V4 In some 50% T may be negative to V6, but in a few weeks it usually becomes positive (2) In later childhood T may be negative to V4 The heart tends to be electrically vertical in children as shown by the patterns of the unipolar leads from the left arm and foot (3) The precordial leads often suggest clockwise rotation round the long axis of the heart High voltages may be due to the thin chest wall

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2 Rossi, E 1954 *Herzkrankheiten im Säuglingsalter*, G Thieme, Stuttgart
3 Goodwin, J F 1952 *Brit Heart J* 14, 173
4 Hollman, A 1958 *Brit Heart J* 20, 129.

Abnormal types. AURICULAR ENLARGEMENT is shown by P waves of high voltage These usually refer to the right auricle The "pulmonary P wave" or "congenital P wave," appears as positive large bifid or prolonged waves in V1 and V2—and also in VF and in VR, where the wave is of course negative This causes large P waves ... sia and the ... and some- ... ey are seen

in transposition of the great vessels. Increased duration of the P wave may suggest that both auricles are enlarged (*1*), as may be the case in atrial septal defect. Abnormalities of the auricular waves are often best seen in the V3R position (*10*). Situs inversus of the heart of course produces a negative P in standard SI, due to the positive P in VR and the negative P in VL.

RIGHT VENTRICULAR ENLARGEMENT. This causes R waves in V1 and V2 (*2*). After the first year the curves are more reliable. It has been suggested that there may be two types (*3, 5*). These depend on whether the hypertrophy is due to obstruction, e.g. pulmonary stenosis (hypertrophie de barrage) or to overfilling (hypertrophie de surcharge) as in atrial septal defect, or anomalous pulmonary veins (*1, 3, 4, 5*). In the latter the curves are of the pattern of right bundle branch block, with a delayed intrinsicoid deflection in V1 and V2 (secondary R wave). In the former there is gross right axis deviation in the standard leads. QRS is not prolonged; the voltages of R in V1 and V2 tend to be high. If these waves are conspicuous a pressure of over 100 mm. Hg is likely to be present in the right ventricle (*10*) In V2, 3, 4 T tends to be negative A dominant R wave is seen in VR A vertical position, with QR pattern in VR, and Rs in V1 is usual (*6*). As time goes on these features become more conspicuous, taking some years to develop (*7*) The curves of right ventricular hypertrophy may be seen in the later years of ventricular septal defect.

LEFT VENTRICULAR ENLARGEMENT may be the cause of left axis deviation and large R waves in V5 and V6 in aortic stenosis. but the vertical position of the heart in early years prevents their appearance The same applies to coarctation of the aorta In tricuspid atresia the unusual combination of cyanosis and left axis deviation is seen This may also occur in persistent truncus arteriosus and in the trilocular heart (*8*)

COMBINED PATTERNS may be seen in the later years of ventricular septal defect and patent ductus arteriosus (*9*), where usually at first the curves are normal The relative degrees of right or left ventricular hypertrophy may decide the patterns of the cardiogram. But diagnosis is difficult. High voltage R waves may appear in V1 and V2 and also in V5 and V6 Mixed types are seen when the ventricular septum is grossly deficient The pattern of the predominance or preponderance of one or other ventricle in the limb leads and the deviation of the electrical axis helps in the solution

In addition to these types suggesting enlargement of one or other ventricle, curves indicating diseases of the myocardium may be

seen when there is an anomalous coronary artery arising from the pulmonary artery, and in fibroelastosis.

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5 Cabrera, E C, Monroy, Y R 1952 *Amer Heart J*. 43, 669
6 Goodwin, J F. 1952. *Brit Heart J*. 14, 173
7 Heim de Balzac, R *et al*. 1954. *Cardiopathies Congénitales*, Paris.
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9 Massio, F *et al* 1955 *Amer Heart J* 49, 188
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CARDIAC CATHETERISATION

Cardiac catheterisation plays an important part in the diagnosis of congenital heart lesions In all but the simplest types it is needed for a precise diagnosis It gives information in three ways: the catheter may take an unusual course by passing through an abnormal orifice in the heart, the pressures in the chambers and vessels accessible to the catheter can be measured, the oxygen content of blood samples can be obtained, and left to right shunts can thus be recognised

METHOD A Cournand catheter of size 5–7 is connected by a three-way tap to a saline drip bottle and via a plastic tube to an electromanometer which transforms the pressures to electrical potentials, these can be recorded on an electrocardiograph The level of the manometer should be brought to that of the right auricle which is taken to be 10 cm above the level of the X-ray table on which the patient lies ...

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The catheter is normally introduced into the median basilic vein. In young children it may be easier to use the femoral ...

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or oxygenated side of the pulmonary system, and the pressures will approximate to those of the left auricle. In practice it is often difficult to obtain satisfactory blood samples from the wedged catheter, nor do the venous pulsations always come through. The catheter is then withdrawn and samples and pressures are taken from the right and left branches of the pulmonary artery, and from the main trunk, from the infundibulum, and from the body of the right ventricle The process is repeated with the right auricle and the superior and inferior venæ cavæ.

Sometimes, especially in mitral stenosis, it is helpful to know the pulmonary arterial pressures and oxygen content after exercise The exercise is performed by the patient pedalling with his feet against resistance while lying on the couch The oxygen consumption can be measured immediately after exercise so that the pulmonary flow can be calculated.

NORMAL PRESSURES. The normal pressures are as follows: right auricle -2 ± 2 mm. Hg, right ventricle, systolic 15–30 mm Hg, diastolic 0, mean pressure 10 mm Hg; pulmonary artery, systolic 15–30 mm. Hg, diastolic 5–10 mm, mean about 14 mm Hg. The pulmonary capillary pressures have a venous form with "a," "c" and "v" waves. The range is from 8–2 mm. Hg *(1)*

Blood samples These are taken under oil so that the oxygen content can be measured. The slightest admixture with air during the drawing of the sample renders it valueless. The oxygen capacity, or the further amount of oxygen which the sample can take up, is obtained and from this the saturation is calculated. The oxygen contents are used to obtain the arterio-venous oxygen difference, and thus to calculate the pulmonary and systemic flows, and so the flow through any shunts that may be present The normal oxygen saturation in the right auricle and right ventricle is about 70% It is slightly higher in the superior vena cava than in the inferior. The different streams of venous blood may mix slowly and the pulmonary artery sample is usually the best to use The oxygen content of the arterial blood is obtained by puncture from the femoral or brachial arteries.

PULMONARY BLOOD FLOW. The volume of blood flowing per minute through the pulmonary system is obtained by the principle of Fick, and is the amount of oxygen taken up by the lungs in cc per minute (O_2 consumption) divided by the difference in the oxygen content per litre in the samples taken from the pulmonary vein and from the pulmonary artery In practice the femoral artery sample is used instead of that from the pulmonary capillary bed as it is

equally oxygenated and is more reliable. The pulmonary flow expresses the output of the right ventricle per minute The systemic flow, and the output of the left ventricle, will be the same, unless

[illegible]

the difference between the mean pulmonary artery pressure and the mean pulmonary capillary pressure by the pulmonary flow. It can be expressed in units (normal 1–2), or in dynes per sec. cm.$^{-5}$ up to 150 dynes, the units being multiplied by 80, or the dynes divided by that factor.

ABNORMAL PASSAGE OF THE CATHETER The catheter, if introduced into the left arm, may enter the chest along an aberrant left superior vena cava collecting blood from some or all of the pulmonary veins It may pass from the right auricle into the left in an atrial septal defect, and thence out into a pulmonary vein (See Fig 8) From the right ventricle it may pass into the aorta in cases of transposition It can very rarely be passed into the over-riding aorta in Fallot's Tetralogy or into the left ventricle through the septal defect From the pulmonary artery it may be manœuvred into the aorta through a patent ductus

ABNORMAL PRESSURES A right ventricular systolic pressure of 45 mm Hg, may be considered as a moderate hypertension, a rise to over 80 mm shows severe hypertension (2) The pressure in the right ventricle may be raised by a variety of causes including pulmonary hypertension, pulmonary valvular stenosis and transposition A moderate rise of hyperkinetic type may be due to an increased flow through a normal valve as in the atrial septal defect, or ventricular septal defect In pulmonary incompetence the diastolic pressure is also somewhat raised

A characteristic curve of right ventricular pressure is recorded in valvular pulmonary stenosis (3) It differs from that obtained in infundibular stenosis In the former the curve is a smooth rounded hump (Fig 11)

The pulmonary pressure is low in pulmonary stenosis, the fall in the systolic pressure being abrupt as the catheter passes beyond the valve less often in infundibular stenosis there is a more gradual fall In pulmonary hypertension due to increase in the pulmonary vascular resistance the pressures are high

LEFT TO RIGHT SHUNTS Left to right shunts are revealed by finding increased oxygenation in the chamber receiving the shunt

and those beyond it. Thus if pulmonary veins drain into an anomalous left superior vena cava, the blood in that vessel will be highly oxygenated and so will the blood in the right auricle and ventricle. In an atrial septal defect the blood in the right auricle will have much more oxygen than in either vena cava In the Maladie de Roger, blood taken from the outflow tract of the right ventricle will be oxygenated while the sample taken near the auricle will not (*4*). In the patent ductus, with a flow from aorta to pulmonary artery, the main branches of the pulmonary artery will be oxygenated.

Complicated formulæ have been made so that the extent of these shunts can be calculated (*5*), but they are only approximate and when the arterio-venous oxygen difference is small they may be grossly inaccurate. It may also be difficult to measure correctly the consumption of oxygen. But they furnish an indication as to whether the shunt is large, moderate or small and are probably worth working out. The formulæ for the septal defects are appended. In the atrial septal defect the shunt in litres per minute equals:

$$\text{Systemic blood flow}\left(\frac{O_2 \text{ in right auricle} - O_2 \text{ in vena cava}}{O_2 \text{ in left auricle} - O_2 \text{ in right auricle}}\right)$$

In the ventricular septal defect the shunt equals.

$$\text{Systemic blood flow}\left(\frac{O_2 \text{ in infundibulum} - O_2 \text{ in right auricle}}{\begin{array}{c}O_2 \text{ in left ventricle} - O_2 \text{ in right ventricle.}\\ \text{(or femoral)}\end{array}}\right)$$

Contra-indications. These are very few. The Ebstein deformity is said to involve risk. Naturally grave heart failure will debar, also pulmonary embolism.

Mishaps are very rare Ventricular premature systoles occur almost constantly when the catheter is in the right ventricle and short runs of ventricular tachycardia are common Transient heart block has been caused. Occasionally there has been hæmoptysis, possibly from too vigorous wedging of the catheter in the pulmonary capillary. Entering the coronary sinus from the right auricle caused temporary precordial pain and collapse in five cases (*6*) But this often happens without harm One patient died following trauma to the right ventricular endocardium near the pulmonary valve (*7*)

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7 Goodwin, J F 1953 *Brit. Heart J.* 15, 330.

ANGIOCARDIOGRAPHY

The opaque substance may show the path of the blood and the outline of the channels it follows 40–50 ml. of 70% Diodone is used If a small amount causes burning in the mouth, the patient is sensitive (*1*) The success of the procedure depends on taking the maximum number of photographs of the circulation in a given time. The difficulty chiefly lies in deciding whether an abnormal outline is due to some deformity in the channel, or to a technical fault. An ideal technique would produce perhaps 8–10 exposures a second from two angles, the right and left anterior oblique positions; a suitable time control should be indicated or the electrocardiogram taken at the same time (*2*) The diodone can be introduced by cardiac catheter to any accessible spot and a selective angiogram taken A right to left atrial shunt may be clearly demonstrated This shows well in tricuspid atresia In the right ventricle the passage of the opaque substance to the left is unlikely to show up well Early filling of the aorta from the right ventricle is a piece of information easily obtained in the Tetralogy of Fallot, and sometimes in the Eisenmenger Complex, or in complete transposition. Dilated bronchial arteries may be seen in pulmonary atresia (*1*) Failure of concentration in the pulmonary artery may be due to blood flowing from a patent ductus arteriosus (*2*). If the ductus flow is reversed this may be demonstrated The right anterior oblique position shows up the infundibulum and pulmonary artery The left anterior oblique is best for septal defects, for the aorta and left main branch of the pulmonary artery (*3*) Coarctation of the aorta may well be outlined in the left anterior oblique position. Other malformations of the aortic arch can be reached by passing the catheter into the carotid artery and using retrograde injection methods Anomalous pulmonary veins are usually well demonstrated (*4*) Arterio-venous fistulæ in lungs are easily seen.

These procedures are not without risk, particularly in [illegible] infants [illegible] is the gr[illegible] volume [illegible], and this method should attempt to answer a question not to be solved in any other way (*5*).

Circulation rate. Estimations are apt to be unreliable; a short arm to tongue time may be found with a large shunt from right to left (*6*).

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DYE DILUTION CURVES

A substance that can be identified, such as Evans blue, or tricarbocyamine when injected instantaneously, is diluted as it circulates, in a specific way. The degree of dilution can be expressed as a curve. The pattern of the curve is altered if there is a shunt, whether veno-arterial or arterio-venous. When there is a shunt from right to left, the dye reaches an oximeter attached to the ear quicker than in normal persons. When a good dilution curve is obtained the results agree with (within about 9%) those obtained by the cardiac catheter as regards the volume of the shunt. The volume of the shunt, as calculated by this method was related to the desaturation of oxygen, as would be expected. If the shunt was more than 35% of the systemic flow the patient was extremely blue at rest. If there is a left to right shunt the appearance time is not altered, but small curves appear in the descending limb owing to late arrival as a result of particles being lost in the pulmonary circulation. Using the cardiac catheter to inject the dye at selected places it may enable more exact localisation of the shunt to be made. Probably these curves will help best when made selectively through the cardiac catheter and for comparing results after operation. The output of the heart can be calculated and the results agree well with Fick's method.

1. Swan, H. J. C. *et al.* 1953. *Circulation*, 8, 70.
2. Shillingford, J. P. 1958. *Brit. Heart J.* 20, 261.
3. Falholt, W., Fabricius, J. 1958. *Brit. Heart J.* 20, 117.

CYANOSIS IN CONGENITAL HEART DISEASE

The cyanosis of some congenital defects of the heart early attracted attention, and acquired its own *name in various languages*

"Morbus Caeruleus," "Maladie Bleu," and "die Blausucht." That it was often due to a shunt was recognised nearly two centuries ago.

Central cyanosis. Cyanosis in congenital heart disease is usually "central" in origin and due to an admixture of venous and arterial blood by means of "shunts" in or near the heart. Central cyanosis differs from peripheral cyanosis in that it is visible in the retina, and inside the eyelids and the mouth The tongue and lips are conspicuously blue, particularly the latter in cold weather. In order that cyanosis be visible, the blood must contain at least 5 grammes of reduced hæmoglobin in 100 cubic centimetres (*1*).

The commonest cause of a shunt of venous blood into the arteries (*right to left shunt*) is a dextroposed aorta drawing blood from each ventricle, in conjunction with a ventricular septal defect and high pressures in the right ventricle This high pressure may be due to pulmonary stenosis as in Fallot's Tetralogy which accounts for the majority of children who are cyanosed from birth or pulmonary hypertension as in the Eisenmenger Complex. In complete transposition of the great vessels all the blood from the right ventricle is delivered into the aorta In a persistent truncus arteriosus, blood from each ventricle is mixed in the common vessel, much the same result is obtained in a large defect in the aorto-pulmonary septum. Gross pulmonary hypertension may cause a reversal of the flow through a patent ductus arteriosus and lead to cyanosis of the lower part of the body Exercise often increases a shunt and so accentuates cyanosis

Peripheral [illegible]

[illegible] If serious failure of the right ventricle comes on, a venous stasis may be present from back pressure Once the tendency to cyanosis is established polycythæmia will be present, and this will increase the actual amount of hæmoglobin, and so raise the proportion which is unsaturated There may be no polycythæmia in children when the arterial blood is only 65% saturated Polycythæmia may, by increasing the viscosity of the blood, interfere with oxygen in the lungs Cold will increase peripheral stagnation and so exaggerate local cyanosis—thus it will often introduce the peripheral factor [illegible]

mc [illegible]

cy [illegible]

th [illegible] The clubbing first appears at the

root of the nail where the sulcus is filled in (2). All stages can be made out up to the typical drum-stick. The flow of blood in the capillaries is slow, and they are turgid and dilated; the retinal veins are very full and dark. The fingers and toes are often long and thin, and so are the hands and feet and arms and legs as well. On the backs of the fingers little veins are conspicuous

There is an increase in the digital arterial pressure which raises the flow of blood per unit of surface in the finger. Clubbing is rarely seen under the age of two years. The bones are not affected Severe cyanosis in infants causes a risk of cerebral thrombosis The increased viscosity of the blood due to the polycythæmia is no doubt a cause (3) Severe cyanosis is often associated with thin and stunted physique, but mental impairment is not a result.

It has been pointed out that *squatting* is an attitude adopted frequently by children with the Tetralogy of Fallot; perhaps some 70% do it (4). It would seem that this position causes slight improvement in the oxygenation of the blood (5). A sort of squatting is seen in the recumbent position, the patient lying doubled up (as noted by William Hunter in 1784). This posture appears to increase the systemic flow of blood. The compression of the abdomen is the point, the arteriovenous oxygen difference in the upper part of the body is lowered (6, 7). In the vertical squatting it is possible that the kinking of the legs at the knees and hips reduces the venous return and increases the flow to the vital centres, for the much desaturated blood is shut off (8).

1. Lundsgaarde, L Van Slyke, 1923. *Medicine*, 2, 1.
2. Lovibond, J. 1938. *Lancet*, 1, 363
3. Taussig, H. B, Blalock, A. 1947. *Amer. Heart J.* 33, 413
4. Wood, P. 1942 *Brit. Heart J.* 4, 11
5. Lequieme, J *et al* 1949 *Cardiologia*, 15, 175
6. Lurie, P. R 1953 *Amer. J Med.* 15, 299
7. Brotmacher, L. 1957 *Brit. Heart J* 19, 559
8. Brotmacher, L 1957. *Brit Heart J* 19, 567

BILOCULAR HEART (COR BILOCULARE)

Cyanosis is present from birth There is a systolic thrill and continuous murmur. The basal second sound is loud The heart is *moderately enlarged.* The high R waves in V1 and VR show clearly There is right axis deviation. P waves are normal

The *angiocardiogram* shows early filling of the aorta and its branches The pulmonary artery fills rather late and the branches

show faintly The septal border of the right ventricle is not defined. *Cardiac catheterisation* shows high pressure in what may appear to be the right ventricle

There may be associated abnormalities, such as pulmonary [illegible]

1. Campbell, M *et al.* 1952 *Brit. Heart J.* 14, 317.

TRILOCULAR HEART (COR BIATRIATUM TRILOCULARE)

When the ventricular septum fails to develop, the heart resembles that of a frog There may be dilatation of the pulmonary artery, which may rupture Cyanosis varies, it may be less than one might expect There is usually some degree of transposition of the aorta and pulmonary artery There is sometimes an abnormality of the outflow tracts to the aorta or pulmonary artery, so that there may be subaortic or subpulmonary stenosis

If cyanosis is present, it tends to increase There is usually a [illegible]

[illegible] cases die in childhood, but adult life has been reached The skiagram is probably fairly characteristic The clinical diagnosis is obviously very difficult

1 Rogers, H M, Edwards, J E. 1951. *Amer. Heart J* 41, 299
2 Richman, B 1950 *Amer Heart J* 39, 887

COR TRIATRIATUM

In this rare abnormality the left auricle is divided into two by a membranous partition, in which is a hole that may be very small Probably the importance of this hole decides the clinical course. If it is large there may be but little ill effect Mitral stenosis may be suspected The right ventricle will be large and the pulmonary pressure raised (*1*)

The heart tends to be globular There are sometimes no murmurs

(2) but a systolic bruit may be heard at the apex (4). If the hole in the abnormal septum is small there will be pulmonary congestion and liability to infection. The enlargement of the heart increases The cardiogram shows right axis deviation; but this may mean nothing in an infant.

It has been suggested that a defect arises late in the second month of fœtal life in connection with the development of the pulmonary veins and auricular septum (3). Surgical treatment might be possible in these cases if the diagnosis could be made This is likely to be done at operation on a case suspected of being congenital mitral stenosis (4).

1. Pedersen, A , Therkelsen, F. 1954. *Amer Heart J.* 47, 676.
2. Barnes, C. G., Finlay, H. V L. 1952. *Brit Heart J.* 14, 283
3. Parsons, F. G. 1950. *Brit. Heart J.* 12, 327.
4. Seavey, P. W., Dorney, E. R. 1958 *Amer. Heart J.* 55, 272.

ISOLATED VENTRICULAR SEPTAL DEFECT (MALADIE DE ROGER)

EMBRYOLOGY. The ventricular septum is formed in its upper and anterior part from the septum which divides the cardiac end of the bulbus cordis. The rest is developed in its lower part from the septum inferius of the ventricle, and from the cushion of the atrial canal in its upper and posterior part The membranous part marks the junction of these two elements The commonest place for an opening is just in front of the membranous part, or near it, but often the membranous part itself is wanting (1, 14) Elsewhere it is rare to find defects, a hole near the apex recalls the heart of the python.

MORBID ANATOMY. The hole may be anything up to a centimetre across, its margin is usually fibrous, unlike the opening in the Tetralogy of Fallot, which is oval with thick fleshy margins On the right side the hole opens under the septal cusp of the tricuspid valve There may be other defects, patent ductus, pulmonary stenosis, and malformation of the aortic cusps There is no set pattern (1). The larger defects over 1·5 cm across are likely to be associated with other abnormalities (14) The aorta tends to be small as in A.S.D., from a decreased flow (14)

HÆMODYNAMICS. The size of the hole will decide the results (8) There will be a flow of blood from left to right This may be anything from 10–15 litres a minute In mild cases when the hole is less

than half a centimetre across, the pulmonary flow may be only 1 5 times the systemic; with a moderate shunt the pulmonary flow is two or three times the systemic; in a severe case it may be three to five times as great. As age increases the associated rise in left ventricular pressure may raise the shunt (*15*)

A small defect may have a normal pressure difference across the septum. Shunts through a hole 0 5 cm. across may be under 25% of total output There is no perceptible increase in the oxygen in the right ventricle, unless the catheter opening taps the stream by luck. Through a hole 1 5–1 8 cm in diameter the shunt may be 4 5 litres per minute. With a large hole the pressures may be more equal, [illegible]

flow to be kept up in the general circulation (*15*).

Arterial blood will be found in the upper part of the right ventricle and in the pulmonary artery. Lower down in the right ventricle the oxygen saturation resembles that found in the right atrium (*3*).

Pulmonary hypertension The pressure in the pulmonary artery tends to be raised in about a quarter of the cases This rise in pressure does not run strictly parallel with the size of the shunt If the hole is more than 1 cm across there is likely to be a rise in pressure in the pulmonary circulation (*4*) Certainly if the hole equals the aorta the pulmonary resistance will be increased (*14*) There may be moderate pulmonary hypertension of hyperkinetic type due to the increased flow, but no actual rise in pulmonary arteriolar resistance (*8*, *15*) Actually the true determining cause of the gross hypertension is the resistance of the pulmonary arterioles These may be thick, with intimal proliferation, perhaps similar to that which is found in some cases with increased inflow from a patent ductus (*4*) But here the severe pulmonary [illegible]

very early, even from bir [illegible]

of the pulmonary arterio [illegible]

(*2*, *8*, *15*) The resistan [illegible]

react to the raised press[illegible] by becoming still thicker (*8*) But in some cases the pulmonary resistance is low (*5*) Even though there is moderate hypertension from increase in flow (*8*)

Clinical features. The signs of the shunt are fairly constant but there [illegible]

hole a [illegible]

other [illegible]

recalle[illegible] these are borne in mind the diagnosis may be made

less frequently than of late. He described "a murmur loud and long. It is single, begins at systole, and is prolonged so as to hide the natural tic-tac. Maximum, neither at the apex, nor at the right base, nor at the left, but in the upper third of the præcordium; it is median like the septum itself; and from this central spot it diminishes evenly in intensity and by degrees, accordingly as one gets farther away from it; it is local and without propagation into the vessels It coincides with no sign of organic disease other than the thrill" Normal at first, later the heart may become enlarged In one series one-third were normal, one-third rather large, and the remainder very large (*15*). The heart beat tends to show increase in vigour. The pulmonary second sound is loud and double, the second element being louder. The pulmonary valves may become incompetent A functional diastolic murmur due to excessive inflow through the mitral valve may be audible at the apex (*8*). A pulmonary systolic murmur may get less as the gradient across the pulmonary valves decreases, or harsher if it becomes larger (*8*).

The skiagram may show a normal outline, but with a large shunt and pulmonary flow, the pulmonary artery and its main branches may be large and pulsate freely (*6*) But further out the constriction of the arterioles may reduce the shadows of the vessels.

The cardiogram is usually normal in early years. With enlargement of the heart the signs of right ventricular hypertrophy may be seen (*7*) This change is likely to be found with pulmonary hypertension If the curve becomes left ventricular in type there is likely to be a large shunt, but no pulmonary hypertension (*8*) Large biphasic QRS deflections appear in V2 to V5 Sometimes there is the pattern of "incomplete right bundle branch block" (*8*).

Prognosis. It seems possible that the hole may close in the first two years of life, but this is not proved It is possible it may get larger (*15*). If the shunt is not too large a normal life may be enjoyed reaching past the age of 50 years In early life there are frequent deaths from failure of the left ventricle (*1*), as many as 70% in the first twelve months If the defect is as large or larger than the aorta, heart failure with pulmonary œdema comes on (*1*) Pregnancy is well tolerated, as in one of Roger's cases, unless the hole is large (*9*). Then the consequences may be serious (*10*)

In young children there may be a type with a large interventricular defect There is the usual murmur, the heart soon becomes much enlarged and grave failure comes on (*11*). Unless, in fact, the hole is small, and there are no other abnormal features bar the murmurs, the prospects are bad and few pass the age of 40 years (*15*)

Associated lesions. Fibrosis around the hole may spread to the aortic valve and cause aortic incompetence. The medial cusp of the tricuspid valve may be deformed. Patent ductus arteriosus may be found There may appear to be pulmonary stenosis, despite this the pulmonary flow may be greater than the systemic so that the vessels of the lungs show normal or increased filling. The pressure gradient across the pulmonary valve may be quite high (*12*). Presumably this is hyperkinetic in origin from the high flow. Infection of the aperture is rare, but some have noted a 25% incidence (*14*) Clinical and catheter evidence point to a possible combination of pulmonary stenosis, ventricular septal defect and aortic incompetence (*17*).

OPERATION With a bloodless field it may be possible to close the defect, if it is thought to be worth while, reasonably safely. A few cases have been done by mattress sutures (*13*). It has been pointed out that the close anatomical relationship of the A-V bundle may be a source of danger at operation (*16*) It is suggested that those with a large shunt and but moderate rise in pulmonary pressure should be selected, not those with very marked pulmonary hypertension (*8*, *14*). The type of cardiogram may help here (*5*). A right ventricular pattern would point to high pulmonary pressure. The left ventricular pattern would favour a large shunt from left to right But all will have had the pressures measured by cardiac catheter

The modern trend of thought is to link up the Roger type of V S D with that included in the syndrome of Eisenmenger. The latter owes its high pulmonary resistance and large pulmonary artery to the persistence of a fœtal condition in the pulmonary arterioles Whether these two are anatomically different, they are *certainly physiologically* similar, and should be thought of together (see p 35)

1 Becu, L. M *et al* 1956 *Circulation*, 14, 349
2 Wood, P *et al* 1954 *Brit Heart J* 16, 387
3 Wood, P 1950 *Brit. med J* 11, 639
4 Joly, F *et al* 1951 *Arch Mal. Cœur*, 44, 602
5 Heath, D 1956 *Brit Heart J*. 18, 1
6 Selzer, A 1949 *Arch int Med* 84, 798.
7 Marsilo, M 1955 *Amer Heart J* 49, 188
8 Blount, S G. *et al* 1955 *Amer J. Med*. 18, 871.
9 Kerr, A, Sodeman, W. A 1951 *Amer Heart J* 42, 436
10 Swan, W C 1952 *Amer Heart J* 43, 900
11 Marquis, R M 1950 *Brit Heart J* 12, 265
12 Curtis, S, Brostoff, C 1955 *Amer Heart J* 50, 513

13. Cooley, D. A. 1955. *Surg. Gyn. Obst.* 101, 153
14 Selzer, A. 1954. *J. Amer. med. Ass.* 154, 129.
15. Brotmacher, L , Campbell, M. 1958 *Brit. Heart J.* 20, 97.
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17. Collins D M *et al.* 1958. *Brit. Heart J.* 20, 363

DEFECTS OF THE AORTIC SEPTUM

Normally the truncus arteriosus is divided by its spiral septum into the aortic and pulmonary artery. Imperfect development of this partition leads to three types of defect.

Persistent truncus arteriosus where there is no septum at all, and the valves are abnormal.

Congenital aortic septal defect, in which the valves are perfect. The defect varies greatly in size.

Aneurysm of the sinus of Valsalva. A local weakness that may rupture

Persistent truncus arteriosus. There is almost always some degree of abnormal torsion If there is a true truncus arteriosus persisting there will be no trace of the pulmonary artery. The pulmonary branches arise from a large trunk guarded by four valves. One pulmonary trunk may arise in this way and divide into two; or there may be one pulmonary branch only The lungs may be entirely supplied by the enlarged bronchial arteries (*1*) The interventricular septum will be incomplete. The heart is usually enlarged. The cardiogram usually shows right ventricular predominance, but there may be left (*2*). The skiagram in young children may be characteristic, resembling a "sitting duck" (Fig. 6). There may be no murmurs, this is the case when cyanosis is intense, but the basal second sound is loud Sometimes there is a murmur like that of a patent ductus, which varies in site and character It is derived from the bronchial arteries, and depends on their size and on the flow of blood through them (*3*) A diastolic murmur may be heard at the apex

The *angiocardiogram* shows immediate filling of the aorta and perhaps the abnormal branches to the lungs In adolescents and later, the pulmonary bow is lacking on the left side, and the two great arteries cannot be distinguished from one another The truncus may run to the right or divide into two, forming a double aortic arch (*2*) The *cardiac catheter* may show a pressure in the right ventricle equal to the systemic arterial pressure (*4*)

Many cases die in early life, but some have reached the age of

thirty. Growth is retarded and the patients are puny. Cyanosis may not always be seen at first, but later it becomes intense

1 Anderson, R C, *et al* 1957. *Circulation*, 16, 586.
2 Rowe, R D, Vlad, P 1953. *Amer. Heart J.* 46, 296
3 Taussig, H B. 1952 *Circulation*, 6, 930
4 Holling, H E, Zak, G. A 1950 *Brit Heart J.* 12, 152.



FIG 6 Persistent truncus arteriosus in an infant

Congenital aortic septal defect. This is found just at the base of the valves, and is due to failure of the aortico-pulmonary septum to unite with the bulbar septum Blood will pass from the aorta into the pulmonary artery causing it to enlarge The hole may develop late in life at an area of thinning [illegible]

[illegible] (3), and even clubbing of the fingers The saturation of oxygen in all limbs is equal The

pulse will be collapsing. The pulmonary vessels will be large and full. The cardiogram may show right or left ventricular preponderance.

The cardiac catheter will show oxygenated blood in the pulmonary artery. The pressure in the pulmonary artery will be high The catheter may pass into the aorta and may be directed up or down (*4*)

The *angiocardiogram* may show opaque material entering the aorta

The differential diagnosis from patent ductus may be very difficult: the murmur and the catheter's point of passage may decide it. It might be possible to close the defect at operation, but the procedure is difficult and dangerous Failure of the right ventricle will come on; sometimes death is sudden

1 Dadds, J. N., Hoyle, C. 1949. *Brit. Heart J.* 11, 390
2. Aubry, J. 1955 *Arch Mal Cœur*, 48, 685
3. Giraud, G. *et al.* 1955. *Arch Mal Cœur*, 48, 567
4. D'Leer, H. A. H., Van Nieuwenhuizen. 1956. *Circulation*, 13, 58.

Aneurysms of the sinus of Valsalva. These usually arise from the right or anterior sinus Rarely does one arise from the left. They may however be multiple and affect all the sinuses The aortic medial coat fails to unite with the aortic ring (*3*) Dilatation of the aortic sinuses may be associated with Marfan's syndrome (*8*) Nomenclature here is erratic The sinuses should be designated as right and left and non-coronary (*4*) Rupture into the right side of the heart is a serious consequence of this lesion The rupture may occur into the right auricle or into the upper part of the right ventricle. The rupture is associated with pain under the sternum and collapse Afterwards a loud murmur, continuous through systole and diastole is heard, resembling that of a patent ductus arteriosus, after a short recovery, failure of the right ventricle ensues. There may be uræmia, a curious finding (*5, 1*) There may be auricular fibrillation heart block may come on Apart from the results of rupture these aneurysms may be associated with aortic incompetence or some slight degree of subaortic stenosis (*1*) The systolic murmur may be quite loud (*6*) Infection is common the murmur may alter and aortic reflux may predominate The aneurysm has been shown by aortography (*2*), or in an angiocardiogram, particularly in left anterior oblique position Other aortic deformities such as mild coarctation may be found (*3*) In the skiagram an aneurysm from the left sinus may resemble a left ventricular aneurysm Surgical

repair by the insertion of a prosthesis has been successfully carried out (7)

1 Morgan Jones, A, Langley, F A. 1949 *Brit. Heart J.* 11, 325
2 Falholt, W., Thomson, G. 1953 *Circulation*, 8, 549
3 Edwards, J. E, Burchell, H. B. 1956. *Proc Mayo Clin*, 31, 407.
4 Steinberg, I. 1956 *Brit. Heart J* 18, 25
5. Oram, S, East, T 1955. *Brit. Heart J.* 17, 541.
6 Steinberg, I, Finby, N. 1956 *Circulation*, 14, 115
7 Morrow, A G *et al* 1957 *Circulation*, 16, 533
8 Steinberg, I *et al* 1957 *Circulation*, 16, 368

TRANSPOSITION OF THE GREAT VESSELS

In complete transposition, the aorta lies in front of the pulmonary artery and arises from the right ventricle, the pulmonary artery lies behind, arising from the left ventricle. Rokitansky in 1875 first supposed that these cases of transposition were due to *anomalous* rotation of the septum which divides the truncus arteriosus Normally, this septum runs a spiral course, finally through 150° in a clockwise sense This is evident when one considers how the pulmonary artery and aorta are wrapped round each other in the normal heart The rotation, or *torsion*, at the distal end of the septum, is at first anti-clockwise to an extent of 180°, later this is followed by a clockwise detorsion of 150° At the proximal end the primary rotation is clockwise to an extent of 90°, followed by an anti-clockwise *detorsion* of 45°. If these processes of torsion are interfered with so that there is less twisting at the distal orifice, and more untwisting at the *proximal*, the ultimate relative positions of the pulmonary artery and *aorta* will be abnormal and some degree of transposition results (Fig 5)

Theories of causation. Keith (1904) stressed the importance of the incomplete absorption of part of the bulbus cordis into the *right* ventricle, as this interferes with torsion Faulty absorption of the bulbus also tends to pulmonary and infundibular stenosis which is usually associated with an over-riding ...

and this is due

suggested that

appeared, while ... primitive reptilian aorta was re-opened on the right side, causing the ...

defect (*12*), the Bing-Taussig syndrome (*1*). These patients are blue early, there is more oxygen in the pulmonary artery blood than in the aorta. *There is no murmur: the cardiogram shows right ventricular* preponderance: the P waves are large (*2*) The lungs are plethoric, the vessels pulsate (*12*).

CORRECTED TRANSPOSITION. Very rarely transposition may be corrected through inversion of the ventricles (*3*). The ventricle which has the form of papillary muscle normally present in the right ventricle is placed on the left, so that the transposition of the great vessels is "corrected" These cases are mainly of pathological interest and not clinically important The aorta then gets oxygenated blood and the pulmonary artery venous.

V.S D. has been noted in these cases of corrected transposition along with complete heart block The association of V.S.D. and complete heart block suggests the possibility of the third feature, corrected transposition. In these instances the V.S.D. was successfully closed with the help of the artificial pump-circulation (*11*).

COMPLETE TRANSPOSITION. If there is no patency of the cardiac septa or ductus arteriosus, the left ventricle pumps blood to the lungs and the right to the body In these circumstances life cannot be maintained There must be associated lesions, such as patent ductus or defect of the cardiac septa. In fact three shunts are possible

(a) *Patent ductus arteriosus* with ventricular septum intact, the foramen ovale being valvular The blood flows from right auricle to left and from pulmonary artery to the descending aorta

(b) *Ventricular septal defect*, the blood flowing from right to left. The blood returns from the lungs either through an *atrial septal defect* or by bronchial veins The lungs are plethoric

(c) *Ventricular septal defect with pulmonary stenosis*, the lung fields being clear (*4*).

Complete transposition. Transposition is not an uncommon form of congenital disease, having an incidence about half that of Fallot's Tetralogy, but most cases die in infancy Boys are more often affected than girls (*4*) Cyanosis is present from birth but varies considerably in intensity Usually the child is stunted, panting and coughing are conspicuous symptoms *The heart is* usually enlarged. Murmurs vary and do not help in the diagnosis There may be a systolic murmur and a loud pulmonary second sound (*5*) In half there are none (*3*) Radiographic appearances also vary greatly. in some the vascular pedicle is narrow since the great vessels lie one behind the other the aorta in front and to the

right of the normal position In some a long bulge is seen in the left middle segment due to the transposed ascending aorta (*1*). Pulmonary plethora may be present The shadows of the vessels in the roots of the lungs may be large, and pulsate freely (5, 6).



FIG 7 Transposition Showing large heart and pulmonary plethora

Angiocardiograms show that the diodrast passes straight up the aorta (7) Electrocard…
The P waves
TRANSPOS…
infancy …
with pa…
to the le…
…ovale, and from the pulmonary

artery to the descending aorta through the ductus, since the pressure in the pulmonary artery, arising from the left ventricle, is high. Oxygenated blood passes down to the legs. In older children cyanosis is invariable with clubbing and polycythæmia, and the finding of a



FIG 8. Transposition Catheter passes through septal defect into left ventricle and out into pulmonary artery.

differential cyanosis with less clubbing of the toes and less cyanosis of the feet than of the hand is diagnostic of this type

TRANSPOSITION WITH SEPTAL DEFECTS Perhaps those do best who have *shunts through atrial and ventricular septal defects* Blood flows from the left to the right auricle and from the right to the left ventricle The lungs are plethoric and the combination of cyanosis and clubbing with *pulmonary plethora is almost diagnostic.*

Cardiac catheterisation. The catheter may pass through the atrial defect and on into the left ventricle whence on occasion it will loop and pass into the pulmonary artery (Fig. 8). If withdrawn it can be introduced into the right ventricle from which it will pass into the aorta The pressures in the right ventricle are high, being about 90 mm (5, 8); in the left ventricle they are low or about 30 mm (5). The oxygen saturation in the left ventricle and pulmonary arteries is 100%; in the right ventricle and aorta it is 70–80% (5)

TRANSPOSITION WITH PULMONARY STENOSIS The flow through the ventricular septal defect is from left to right and the lungs are clear (*4*). The blood supply to the lungs is maintained by large bronchial arteries, and this may be suggested by a systolic murmur audible between the shoulder blades (*10*)

Auriculoventricular dissociation may occur In one case huge auricular waves were seen, varying from beat to beat. The right auricle was hypertrophic (9).

No surgical correction is possible in transposition because of the position of the coronary arteries Transposing the great veins is a possibility but has not so far been attempted (*4*)

1 Taussig, H. B, Bing, R J 1949 *Amer Heart J* 37, 551
2. Azevedo, C *et al* 1956 *Amer Heart J.* 52, 2, 49
3 Cardell, B S 1956 *Brit Heart J* 18, 186
4 Astley, R, Parsons, C 1952 *Brit Heart J.* 14, 13
5 Keith, J D. *et al* 1953 *Circulation*, 7, 830
6. Campbell, M., Suzman, S 1951 *Circulation*, 4, 329
7 Goodwin, J F *et al* 1949 *Brit Heart J* 11, 279
8. Wood, P 1950 *Brit med J* 2, 693
9 Aitchison, J. D *et al* 1955 *Brit Heart J* 17, 63
10 Cudkowitz, L, Armstrong, J B 1952 *Brit Heart J.* 14, 374
11 Weldon, J W *et al* 1958 *Circulation*, 17, 249.
12 Chiechi, M A. 1957 *Amer J. Med* 22, 234

TETRALOGY OF FALLOT

The commonest congenital defect in which cyanosis is conspicuous is the combination of lesions to which the name of Fallot (1888) has been attached This was well described by Peacock, the English physician, in 1866 The tetralogy consists of

1. Dextroposition of the aorta.
2. Stenosis, hypoplasia or atresia of the pulmonary artery
3. Interventricular septal defect.
4. Hypertrophy of the right ventricle

Morbid anatomy. Pathogenesis. The abnormality arises in the fifth week of fœtal life. At this time, the torsion of the primitive bulb is taking place to bring the aortic part round, and forwards and to the left in an anti-clockwise direction; and also the primitive tube is being divided by the spiral septum into aorta and pulmonary artery; the septum between the ventricles is growing upwards to meet that of the bulb It is clear therefore that if the correct degree of torsion fails to occur, the aorta remains too far to the right, and the union of the ventricular and bulbar septa does not take place. Incomplete absorption of the bulb causes a varying degree of pulmonary stenosis.

RESULTS. The degree of *dextroposition* of the aorta varies a good deal: it may be easily apparent on the screen when the heart is viewed from the front. At autopsy even, it may be difficult to say exactly how much the aorta was out of position. It is usually rather large, but narrows after the left subclavian leaves it (*24*) Possibly the dextroposition is not very important if slight in degree

The STENOSIS of the pulmonary orifice varies too. About half are probably infundibular, while a combination of infundibular and valvular may be met with in some 15% About 30% are purely valvular There may be only two cusps in about half of these. a few may show a conical opening The pulmonary artery is about half the size of the aorta (*24*) in contrast to its increased size in the simple uncomplicated valvular stenosis

The SEPTAL DEFECT is fairly constant in form but may vary in

across or a good deal larger (*1*).

With this degree of variability in the four features patients may vary a good deal. At one end of the scale is the case with fairly severe pulmonary stenosis and large septal defect, so that the ventricular pressures are equal and the patient very blue, at the other end is the case without cyanosis where the septal defect is small and the pulmonary stenosis severe, yet with small right to left shunt, or the combination of large septal defect and slight pulmonary stenosis with left to right shunt, and again no cyanosis (*19*). In about one-third there is a functionally patent hole between the auricles, but this is not of much importance

CLINICAL FEATURES These are well known Cyanosis is usually present from birth, or develops in the first year (*2*) Physical development is often retarded, so that the child grows up small and

puny. Mental development is quite unaffected. Physical activity is much reduced as a rule; there is a pronounced tendency to adopt the squatting position The standing position is detrimental, and squatting seems to help venous return (3) (see p. 16). The children often lie curled up (26). As usual the cyanosis is associated with polycythæmia and clubbing of the fingers and toes. Arachnodactyly [illegible]

increased cyanosis, the blood pressure does not fall: the right to left shunt is much increased The pulmonary stenotic murmur tends to fade It has been suggested that contraction of the infundibulum obstructs the flow of blood to the lungs and so leads to more anoxæmia and a loss of consciousness Cyclopropane seems to relieve the spasm (29)

The size of the heart shadow may not be increased when seen *from the front, but there is clinical evidence of the hypertrophy of* the right ventricle in the beat

The systolic murmur is loud, and best heard in the 3rd, 4th and 5th spaces to the left of the sternum There is usually a thrill with it It comes soon after the first sound and is maximal at once The second sound at the base may be loud, derived mainly from the aorta, which lies to the front (4, 5) Occasionally the second sound is double, the second faint component being pulmonary (5) The cyanosis is due to the free flow of venous blood up the dextroposed aorta The oxygen saturation of arterial blood is anything from 60–80% Estimation of the rate of the circulation will show a very short time from arm to tongue, owing to the direct flow up the aorta The systemic blood flow at rest is within normal range, but the pulmonary flow is reduced by the amount of shunt from right to left (6)

Examination with X-rays shows oligæmia of the lung fields The pulmonary conus is small or absent The true "Sabot" appearance is best seen in children, and may be wanting in adults The dextroposition of the aorta is an important point in diagnosis if it can be made out In about one-third of cases the aortic arch is right-sided (1), as was first noted by Corvisart This anomaly is obviously important when the Blalock operation is being [illegible]

The ar[illegible]

aorta T[illegible]

but this negative finding may be due to technical causes, and so

unreliable (*7*). The pulmonary artery, if shown, may appear to be further to the left than normal (*4*, *8*). There may be associated anomalies of the pulmonary and its branches, one main branch being closed and the other large (*9*). The pulmonary main trunk may be short and run backwards (*8*).

The *cardiogram* tends to show pointed P waves *of high voltage* (*2*). It may be noted here in this context that the auricular "a" waves

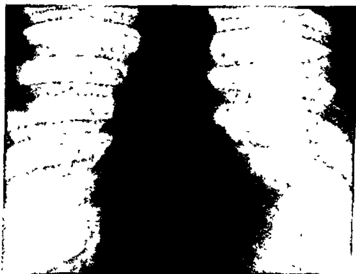


FIG. 9 Tetralogy of Fallot

in the jugular veins are not large (*4*). There is usually right ventricular preponderance, the intrinsic deflection on the right side may be a little delayed, but not to the full degree of typical "right bundle branch block" (*11*, *13*) This contrasts with the curve of atrial septal defect when considerable delay in activation is the rule [illegible] de surcharge). The curve also differs from that usually [illegible] To the [illegible]

The *cardiac catheter* shows that the pressure in the right ventricle is raised. It may be quite high, perhaps 80–90 mm Hg, thrice the normal. The pressure in the pulmonary artery is low and the pulsations small The change from ventricular to pulmonary pressure may be sudden if the stenosis is valvular, or gradual if infundibular. On some occasions the catheter may pass up the

aorta, or through a foramen ovale. (For the differential diagnosis see p 37)

INDICATIONS FOR OPERATION. The optimum time is between 8 and 14 years (*21*). But the general state of the child's health and development must be considered. The degree of cyanosis (arterial oxygen saturation) and the grade of the pulmonary oligæmia are the most important special points Syncopal attacks and grave physical disability would indicate operation as soon as it can be done (*21*).

OPERATION In the operation of Blalock a left lateral incision is used and the left (or right) subclavian artery is joined to the left (or right) pulmonary artery, whichever suits better, by lateral

The cyanosis may disappear entirely, or only be seen on exertion The hæmoglobin may fall to nearly normal levels and clubbing disappear Squatting is no longer seen (7) A five-year follow-up of nearly 250 cases shows 95% good results, that is, the hæmoglobin was normal and there were no restrictions on life's activities The "Gibson" murmur usually persisted. The enlargement noted

of the cases, and "good" in another smaller group The mortality was just over one in ten (*14*). Similar results have been reported in other series (*15*, *16*).

For comparison the results of valvotomy or infundibular resection (Brock's operation) are interesting Here again two-thirds got very good results Mortality was about 15% Failure of the ventricle has been noted due to pulmonary regurgitation and because the shunt from left to right increased when the pressure in the right ventricle fell (*25*) Actually valvotomy is rather safer than infundibular resection (*17*) After this operation there may be some increase in the size of the heart as after the Blalock

to survive past middle age, but they were very exceptional; most lived restricted, invalid lives and died young. *An interesting point* is the unilateral notching of the ribs due to reversed collateral circulation to the arm after the subclavian artery on that side has been divided (*27, 28*). The blood returns through the intercostals to the internal mammary and so to branches of the axillary artery.

ATYPICAL CASES. It has long been known that some are not cyanosed to begin with; and it is possible that this combination of lesions or something like it may exist without the patient ever becoming blue These patients do not require operation. In these cases a loud systolic murmur and a thrill in the third left space have been described; neither ventricle is obviously enlarged; the pressure in the right ventricle is high equalling that of the systemic circulation; the pressure in the pulmonary artery is low or normal. There is a ventricular septal defect, the cardiogram suggests slight preponderance of the right ventricle (*20*). Fuller findings post mortem would be interesting.

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2. Baker, C *et al.* 1949 *Brit. Heart J* 11, 170
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17. Campbell, M *et al* 1954 *Brit. med J* 11, 112
18. Liniger, C R 1951. *Amer J Dis Child* 61, 465
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22. White, B D *et al.* 1956. *Circulation*, 14, 512
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25. Lin, T. K. *et al* 1958 *Amer. Heart J* 55, 288
26. Brotmacher, L. 1957. *Brit Heart J.* 19, 559, 567
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29. Wood, P. 1958. *Brit Heart J* 20, 282.

Pulmonary atresia. The pulmonary orifice may be closed at the valves (*1*) and the artery thin and hypoplastic above, or the maldevelopment may affect the whole of the infundibulum and pulmonary trunk In the latter the sixth left arch has disappeared and the ductus is closed. Otherwise the ductus may be patent and supply blood to the lungs These patients are very blue, the arterial saturation being some 60–70%, but not necessarily severely incapacitated nor stunted in growth The signs are variable. In some no murmur is audible at all, and this serves to distinguish them from the Tetralogy This they resemble in that there is a hollow concavity in place of the pulmonary bulge. If the lungs are supplied by large bronchial arteries these may make no murmur, but in some cases a continuous murmur is heard between the scapulæ This may vary and later disappear. In the skiagram the irregular shadows of the bronchial arteries may be seen, arising from the aorta; they are sometimes nodular and lie apart from the heart (2) There is a patent atrial septum in a fairly large number of cases. The question whether a Blalock operation should be done in these cases needs careful consider...

... may be very unsuitable to receive the subclavian artery.

1 Allenby, K W *et al* 1950 *Guy's Hosp. Rep.* 99, 110.
2 Campbell, M , Gardner, F 1950 *Brit Heart J* 12, 184.

EISENMENGER COMPLEX (1897)

This is a rare finding. As there is some degree of dextroposition of the aorta and a large crescentic hole in the top of the interventricular septum with a thick muscular lower margin, it would seem that this combination of defect may be related to the Tetralogy of Fallot The aorta may be small, and sometimes there is a true right-sided arch The inference is that there is some defect ...

... (1) The artery may become so large that the valves are incompetent

MORBID ANATOMY AND PHYSIOLOGY The most remarkable feature of the cases is a high pressure in the right ventricle and

pulmonary artery. The cardiac catheter shows that this may range at systole from 75 to 150 mm. Hg (*2, 3, 4*). The cause of this hypertension lies in the pulmonary bed where the resistance may be very much increased, reaching 1700 or 2500 dynes, some ten times the normal (*5, 6*). The increased resistance is associated with hypertrophy of the muscular coats of the arterioles and proliferation of their intima (*2, 3*). The latter is more conspicuous (*12*). The pressures in the pulmonary capillaries and veins are normal (*5*). It would seem possible that increase of tone in the pulmonary arterioles causes their hypertrophy, as in systemic hypertension; some think that these are developmental abnormalities and due to failure of [illegible]

bed from too great a flow. The result is that although the pulsation of the pulmonary artery as viewed on the screen may be increased, *that of the branches is diminished, and the smaller branches seem* empty. The pulmonary flow is actually reduced, even to one-third (*1, 9*) Hæmoptysis is common and there may be pulmonary thrombosis (*3*).

The position of the aorta, somewhat to the *right*, over-riding the interventricular septum, favours a shunt from right to left, and this is further provoked by the high pressure in the right ventricle which may equal that in the left Probably the pressure rather than the position of the aorta matters more. The tricuspid leaflet may close the septal defect and prevent cyanosis (*12*) There is considerable hypertrophy of the right ventricle.

CLINICAL FEATURES Cyanosis is variable both in degree and time of onset. It usually comes on late but some are blue at birth Exercise may provoke cyanosis Clubbing of the fingers and polycythæmia run parallel with the cyanosis, as usual Once cyanosis has developed it tends to become more severe as years go by. The oxygen saturation of the arterial blood may be 75–80% (*5*). *The tendency for a left to right shunt between the ventricles* is small as a rule, but sometimes the cardiac catheter withdraws well-oxygenated blood from the right ventricle (*8*) The auricular (a) waves in the external jugular veins are often large, as *is the rule in* pulmonary hypertension (*2*) There is the usual strong impulse over the right ventricle to the left of the sternum There may be dullness to the right. Pulsation can be felt over the pulmonary artery where there is usually a loud systolic murmur and sometimes a thrill The closure of the pulmonary valve can be felt, and on auscultation there is wide splitting of the second sounds, the

pulmonary component being the louder. The diastolic murmur of pulmonary incompetence may be audible (*10*) The circulation time from arm to face is short, for the lungs are by-passed (*11*).

X-ray examination shows the large pulsating pulmonary artery while the smaller branches seem poorly filled The angiocardiogram will show early filling of the aorta and its dextroposition. The pulmonary artery empties slowly (*1*).



FIG 10 Eisenmenger Complex

The cardiogram shows right ventricular hypertrophy, or the pattern of "incomplete right bundle branch block," indicated by delayed activation of the surface of the right ventricle

...ase of patent ductus is that there is much more pulsation in the pulmonary artery and its branches Idiopathic pulmonary hypertension may *resemble* Eisenmenger's Complex in the late stages but the cyanosis is less severe and ...

...ale Aortic reflux points rather to V S D. Anomalous pulmonary veins go with A S D The problem may be far from easy (*16*).

COURSE AND PROGNOSIS. Sooner or later failure of the right ventricle with increasing cyanosis comes on: few cases pass middle age. Although at first there is but little disability the bad effects steadily increase *Thrombosis of the branches of the pulmonary* artery may hasten the end. If the pulmonary valves become incompetent the right ventricle fails the sooner. Once started the failure tends to progress rapidly (*12*).

Conclusion. It seems likely that at the one end of the scale is the simple Roger type, with small hole and not much shunt. At the other is the Eisenmenger type with large shunt, high pulmonary arteriolar resistance dating from early years, leading to rise in pressure in the right ventricle and reversal of the shunt with cyanosis. Between these two lie varying grades. The rise in pressure on the right side may at first be hyperkinetic if the shunt is large, later it is aggravated by obstruction The size of the hole, the pressure on either side, the volume of the shunt and its direction are the variable factors. Cyanotic or acyanotic they are all in one group (*13, 14, 15*) (see also p. 21). The position of the aorta is not functionally *important. A wider view regards the important point as a large hole* between the two circulations and the reaction of the pulmonary bed to it, so that it may be called a syndrome (*17*).

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4 Kohout, F W *et al* 1955 *Amer Heart J* 50, 337
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PULMONARY STENOSIS (ISOLATED)

This lesion may be further defined as a stenosis at the pulmonary orifice with the aorta in a normal position (*1*) As a rule it is to be added that the septum between the ventricles is closed, but it will be seen later there are certain cases in which there is a small hole

with the shunt from left to right Probably cases of pure stenosis comprise about 10% of all types of congenital heart disease (2). The sexes are equally affected

MORBID ANATOMY. The stenosis is valvular in perhaps 80% of cases Here the valves are fused to form a diaphragm which is often like a dome, with a small hole in the centre Fibrosis may extend into the muscle of the conus adjacent. The absence of a hole between the ventricles in most cases suggests that the lesion forms after the eighth week of fœtal life.

The *infundibular defect* goes back earlier in fœtal life Keith has explained this lesion as the result of a failure of the bulbus cordis

...er occupies

...he enlarged

The lining of the chamber is usually thickened A large crista supraventricularis may cause obstruction (35) The pulmonary artery above the valves is usually enlarged, particularly in the valvular type, its walls are thin The enlargement may extend to the main branches There is no relationship between this enlargement and the degree of

... It seems to have a

...The small vessels in

...may be narrowing

...valve. Sometimes

there are multiple constrictions, some long, some short (*34*). As a result of the stenosis the right ventricle is hypertrophied.

HÆMODYNAMICS There is a rise in pressure in the right ventricle This may reach nearly *200 mm* Hg In milder cases the pressure ranges between 50 and 100 *mm* Hg. An average between 70 and 80 is common (5) The *sudden* change from the very small waves

ve...

...more likely to be infundibular (Fig 12) If the tip of the catheter is watched during its passage an exact interpretation can be obtained The raised pressure in the right ventricle causes large "a" waves of auricular systole in the veins of the neck (*1, 3*) The pulmonary flow may be normal if the stenosis is slight (2) The cardiac catheter does no harm, it would seem, although it might theoretically aggravate the stenosis when in the pulmonary orifice In the infundibular lesion a pressure tracing taken in the ventricle and in the infundibulum may be synchronous or asynchronous as timed against the ECG ventricular deflection If the former, there is a fibrous opening from the

ventricle and not a muscular ring If the ventricular pressure goes on rising, after this peak of pressure in the infundibulum, the orifice is muscular and contractile, and easier for operation (*33*)

Angiocardiograms. These show slow emptying of the right auricle and ventricle (*6, 7*). At the pulmonary orifice the deformed valves may show up, or the narrow infundibulum. As these are negative findings the shadows are apt to be deceptive, for technical variations

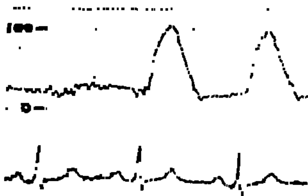


FIG 11 Pulmonary valvular stenosis.

may cause them When the large pulmonary artery is full it shows up well.

The ordinary skiagram of the lungs shows oligæmia as a rule, but there is a good deal of variation The trunk of the pulmonary artery does not pulsate

CLINICAL FEATURES About a quarter of all cases have no symptoms. The complaint is usually fatigue, dyspnœa, and cyanosis The pressure in the right ventricle does not correlate closely with the symptoms. Cyanosis suggests a severe obstruction The highest pressures go with the smallest pulmonary orifices There is fair correlation between this pressure in the right ventricle and the cardiogram With a systolic pressure above 100 mm. Hg, R in V1 and V4R exceeded 20 mm and a pulmonary P wave was seen Over the right ventricle the S-T interval and T waves were abnormal (*37*).

The face is sometimes full and bloated Large "a" waves are seen in the veins in the neck. There may be precordial pain of anginal type which nitro-glycerine can relieve Fibrosis of the right ventricle was found (*8*).

The large right ventricle is indicated by the strong lifting impulse

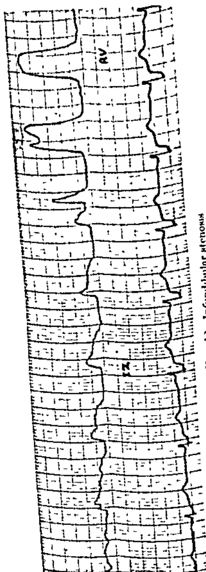


FIG 12 Infundibular stenosis

to the left of the sternum. There may be some dullness to the right if the right auricle is enlarged. Over the pulmonary valves there is the characteristic harsh systolic murmur of stenosis with a thrill When there is stenosis beyond the valves the murmur may be prolonged, rather like the Gibson type (*34*). The pulmonary second



FIG. 13 Pulmonary stenosis (valvular) Note large pulmonary artery and oligæmic lungs

sound is abnormally soft and as usual, will follow the sound of the closure of the aortic valves Some think that infundibular stenosis has the murmur lower down This is hard to be sure of in a small child. Cyanosis may be absent When the cardiac septa are closed peripheral cyanosis may be noted later If failure has come on this may be severe (*8*) There is some evidence that the flow in the body may be of unusual distribution, namely an extra large flow down the superior vena cava while that to the upper part of the body is increased in some way, thus favouring the vital centres (*9*) The oxygen content of the I.V.C blood is usually 4% higher than

that of the S V C. In pure pulmonary stenosis the S.V.C. has a higher O_2 content, as normally occurs.

Patent interatrial septum. The rising pressure on the right side of the heart may open a valvular foramen ovale and permit a shunt from right to left. This will cause central cyanosis which may become severe Along with this signs of right ventricular failure may appear On the other hand there may be a true atrial septal defect, which in France constitutes the Triad of Fallot. With this the cyanosis may come earlier as only a small rise in auricular pressure will reverse the shunt Some are blue at birth; transient cyanosis tends to become permanent (*27*) The shunt may amount to over 4 litres a minute (*10*). In some cases it was 50% or more of the systemic flow (*27*) In some patients the left ventricle is enlarged. This is said to be [illegible]

[illegible]

more puny and weak In the Trilogy cyanosis is more obviously increased on exertion, the hæmoglobin 120%, or less The signs of the Trilogy are more conspicuous The "a" waves are large, the *murmur is* louder, the second sound more split on inspiration; the aortic second sound is not so loud (*33*)

The skiagram of Fallot shows no enlargement, whereas at this stage in the other the increase is severe The pulmonary arc of Fallot is wanting in *the other* the artery is large and the lungs less oligæmic Some 25% of the Tetralogy have a right-sided aortic arch it is *rare in* pulmonary stenosis The cardiogram shows preponderance of the right ventricle in both, but the evidence of strain is more *marked in* pulmonary stenosis, T waves being negative to V4 lead The right *ventricular* pressure equals the systemic in Fallot's Tetralogy, in the pulmonary stenosis it reaches higher levels An infundibular withdrawal curve favours the Tetralogy Diodrast will pass through the A S D and show the shunt from right atrium to left; in Fallot's Tetralogy it will fill the aorta [illegible]

(hypertrophie de barrage). The P waves tend to be of high voltage (*11*). The P-R interval may be prolonged. The P waves in the standard II lead may be large (*3*). The correlation with the R-V pressure has been mentioned.

Mild cases of pulmonary stenosis with closed septa. These have the thrill and murmur. One may suspect that the dilated pulmonary artery enhances them. But the right ventricle is only a little enlarged and the right auricle not at all. The electrocardiograms show some slight right ventricular predominance. Pressures in the right ventricle are but little increased and the curve from the pulmonary artery is of the usual arterial type. The pulmonary vessels are well filled These patients have no symptoms No operation is needed for them (*12*, *13*)

Prognosis. In the mild cases this is good, and some reach old age. In one patient nearly sixty, the pressure in the right ventricle was not over 100 mm. Hg and the cardiac output at rest was normal (*28*) If, however, cyanosis develops, central in type, the outlook is bad. Once heart failure has come on it progresses fast. The hole does not increase in size, so the growth of the body at puberty makes the defect relatively worse (*14*). Bacterial infection may occur Phthisis is not uncommon.

Operation. For the valvular stenosis or for the infundibular the operations devised by Brock (*16*) may have brilliant results

The pressure in the right ventricle may fall to half its former level, and the interatrial shunt from right to left, if present, disappears so that cyanosis vanishes (*15*) Even gross failure may clear up. The cardiogram becomes more normal, improving even in a few days (*36*) The heart decreases in size and the pulmonary vessels seem better filled The murmur and thrill may remain unaltered The infundibular lesion is of course more difficult to enlarge, but even after full dilatation the pressure in the right ventricle may not fall much During operation various ventricular arrhythmias may be noted, from extrasystoles to tachycardia—variation in pacemaker is seen and A-V block Bradycardia is ominous (*18*) In skilled hands mortality is small, particularly if failure has not come on With safe hypothermia or alternative extra-corporeal circulation, results should be better. The direct attack has advantages The closed method is not so good (*36*) It is so important to know how much of the obstruction is valvular and how much infundibular Time is needed and if available, septal defects if present can also be repaired (*37*). A plastic operation on the valve can be done. There may be some pulmonary reflux afterwards (*28*).

INDICATIONS FOR OPERATION. Increasing cyanosis, central or peripheral is an important point. Mild cases can be left, the right ventricular pressure being but little raised and the cardiogram normal (*37*) If the mean right ventricular pressure is 70 mm. Hg or more, the operation should be done (*19*), certainly if over 100 mm Hg (*32, 37*) The moment deterioration threatens, that is to say symptoms appear where none were before, operation should not be delayed Any increase in the abnormality of the cardiogram would be a point in favour (*20*), as would an increase in size of the right ventricle, which may become enormous. The cardiogram may be unreliable in young children (*35*) The point is that operation should not be delayed lest it be too late.

Pulmonary stenosis with ventricular septal defect. Left to right shunt may occur (*1*) These cases are unlike the Tetralogy of Fallot, for the aorta is not dextroposed and the ventricular septal defect is small The signs of pulmonary stenosis are present, which may be valvular or infundibular, as the catheter may suggest (*23*). The pulmonary artery pulsates freely and the flow into the pulmonary circulation is not much reduced. The pressure in the right ventricle is but moderately raised The diagnosis depends finally on the detection of arterial blood in the right ventricle The cardiogram may be of the R bundle branch block type; pronounced right ventricular predominance is not always seen (*21, 22*). Exercise may reverse the shunt and cause cyanosis

As in these cases the stenosis is probably slight and the increased inflow is responsible for the hypertrophy of the right ventricle as much as the stenosis, one may look on this as largely relative Valvotomy is not needed here The best procedure would be to close the septal defect (*24*) if that were possible It would appear that this combination may be present with aortic reflux (*40*)

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CONGENITAL AORTIC STENOSIS

It is convenient to consider the two types together although they are of different origin, and are also different from the point of view of operation

Valvular type. In this type the lesion is at the valves, and the defect is homologous to the valvular type of pulmonary stenosis. The valves appear to be fused and thickened, this state apparently results from faulty development, it may lead to incompetence of the valves. Three-quarters of the cases are males (*1*) The pulse is small and anacrotic, and the pulse pressure is low, but there is variation (*11*) The valve must be reduced in size to below half its area before the circulation is affected (*1*) The rough harsh systolic murmur conducted to the neck is obvious, and there is usually a systolic thrill

The character of the aortic second sound varies and is unreliable (*11*) It can be quite normal and even loud (*2, 3*) Probably in about half it is weak (*1*) *Calcification does not reduce it necessarily* (*4*)

Enlargement of the heart may be slight or inconspicuous, this may be due to its vertical position in children Above the valves the aorta may be dilated as in pulmonary stenosis. This helps to distinguish from the subaortic type but is not a reliable feature. As the left ventricle enlarges the T wave over it may become negative.

Subaortic type. This is probably rare and is usually not severe (2, 8) The lesion is due to imperfect involution of that part of the bulbus cordis which takes part in the formation of the left ventricle just below the valves. The defect is homologous to conus or infundibular stenosis in the right ventricle, into which most of the bulbus is absorbed A fibrous ridge or bar is seen just below the semilunar valves, which contains a good deal of elastic tissue Calcification is less likely than in the valvular type, over the age of thirty Occasionally there may be stenosis of the valves as well, as on the pulmonary side Coarctation may be present in the aorta. The usual systolic murmur and thrill are produced, but the obstruction is not often severe enough to cause much left ventricular hypertrophy, so the cardiogram may not show left ventricular predominance For the same reason the anacrotic type of pulse is not felt, and the blood pressure may not be low It is doubtful whether variations in the second sound help in the diagnosis from the valvular lesion (3) Angiocardiography might help [illegible] the extent and site of the [illegible] injected through a wide [illegible] and rapid pictures taken in the left lateral position But really it might be necessary to inject directly into the left ventricle (13) A notch on the downstroke of the subclavian pulse is said to show that the valves are mobile (8) This type of stenosis is not so suitable for *operation*

Surgical *treatment*. The operation is still one of rather high mortality, but the cases vary a great deal in gravity No doubt the results will be better as the selection of cases improves If the valves are severely calcified and densely fused the difficulties may be greater, but gross calcification will not be seen early The hypertrophied left ventricle is irritable (6) It is important to decide on operation before heart failure comes on Dyspnœa, syncope and giddiness together with the cardiographic evidence of left ventricular strain indicate *operation* (2) Aorta reflux may result from the operation but this should be less likely in the subaortic type How far the grave risk of infection is minimised is doubtful Estimation of the pressure in the left ventricle, by direct puncture through the chest wall may be done It does not seem risky It is possible to

catheterise the left side of the heart through the left main bronchus, which is in direct relation to the left auricle. This method is relatively safe as the pericardial sac is not entered (*14*). The puncture of the left auricle directly through the skin of the back is less easy and by no means free from risk (*15*). Probably the most practical way is to get the pressure at the time of operation: but the information is really needed before the chest is opened (*16*). The knowledge of the pressure gradient across the aortic valves is most important The physical signs may be very deceptive as to this essential point (*10*). About 50 mm. Hg of differential pressure indicates operation (*11, 17*) The possibilities of a dry field are very important; how far hypothermia or an artificial heart is better remains to be seen. No doubt the difficulties of the transventricular route will be made less. It is however preferred where there is calcification (*10*).

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EBSTEIN'S DEFORMITY (*1866*)

Morbid anatomy. There is a deformity of the cusps of the tricuspid valve. These are fused and drawn down into the ventricle. The posterior cusp is most abnormal, the septal may be well formed. There may be a good deal of fenestration, the papillary muscles are deformed. The attachment of the valve flaps spreads downwards into the ventricle which is divided into two chambers, a relatively small outflow tract, and the part above the valve where the wall is very thin and resembles that of the auricle. This atrophic muscle is held to be the result of the deformity (*1*). This chamber is very large, and may become enormous. The upper part of the right

ventricle is actually auricular in function. The foramen ovale is usually patent, or there may be an atrial septal defect; then the hole is large

appear fairly late, and its degree will depend on the size of the atrial septal defect (*3, 4*) It varies a good deal (*11*), and may increase with exercise (*12*) The femoral arterial oxygen saturation may be about 80% (*2*) There may be clubbing of the fingers, and the usual polycythæmia Dyspnœa of varying degree is the dominant symptom, but it may be mild Squatting is unusual The heart is enlarged, particularly to the right, and looks globular (*10*) A systolic murmur which varies a good deal is usually audible near the lower end of the sternum There may be a diastolic murmur (*11*). A gallop rhythm is often noted (*3, 4*).

The cardiogram may show a prolonged auriculo-ventricular conduction (*3, 5, 6*) The P wave is usually of high voltage, large and peaked in V1 and V2 (*13*) The QRS complex is usually of the right bundle branch block type (*3*), but the left-sided variety may occur Normally in health the voltage of R over the right ventricle tends to be low, when it is high over the left ventricle it suggests enlargement here (*5*) Auricular fibrillation and auricular tachycardia occur (*12, 13*) The angiocardiogram shows the large right auricle which empties slowly (*2, 3, 6, 7*), the left filling at the same time (*10*) The tricuspid notch is wanting, the pulmonary artery may not fill or the pulmonary artery and the aorta may fill together (*9*) The cardiac catheter may pass through the hole in the atrial septum The pressure in the right auricle may be the same as that ...

... at the bottom of the outflow tract Catheterisation may be dangerous, though some do not think so (*10*), there may be some risk of producing arrhythmia and of perforating the thin wall of the ventricle or of damaging the tricuspid valve (*3*) The lungs may be oligæmic, or show slight congestion The circulation time is prolonged (*2*).

COURSE AND PROGNOSIS. Failure of the right ventricle is likely to come on The liver becomes large and pulsating Some patients

have reached the twenties and thirties. Pulmonary tuberculosis is common.

DIAGNOSIS. This is very difficult as the cases vary so much. The important features are the huge right auricle, and as a rule the right ventricular type of cardiogram, and sometimes oligæmic lungs (*10*). It is important to distinguish this from the Tetralogy of Fallot, where operation may help, for here it cannot do so. The late onset of cyanosis is a point, but this may be the case in the Tetralogy. The Triad of Fallot should present no difficulty with its high right ventricular pressure and signs of pulmonary stenosis, together with right ventricular enlargement

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TRICUSPID ATRESIA

This cyanotic lesion has lately attracted attention, it is important to distinguish it from those for which there is some effective surgical treatment

MORBID ANATOMY. The valve and right ventricle may be wanting, or they may be present in miniature form Infundibular stenosis, if there is a pulmonary artery, may be present (*1*) This part may communicate with the left ventricle through a hole high in the septum The valves may be bicuspid The right ventricle may be *in two parts (2)* Sometimes there is transposition of the great vessels. These defects arise very early in fœtal life, in the fourth week, so the association of the other lesions is likely (*3*)

HÆMODYNAMICS. The blood must reach the left side of the heart through a defect in the atrial septum which may be the foramen ovale or one of the other apertures The final path to the lungs may

be through a ventricular septal defect into the small right ventricle and up a stenosed pulmonary artery; or if this channel is closed, by a patent ductus, or through bronchial arteries (4) The pulmonary flow tends to be small.

CLINICAL PICTURE Cyanosis is usually intense and is apparent at birth, or appears soon after. A few are not blue if transposition allows blood from the left ventricle to flow direct to the lungs. The baby is wasted and puny and liable to dyspnœa Many die in the first year of life; a few may live longer (1, 5), but not many pass seven years. There is usually a loud systolic murmur and a thrill (6) [illegible] he veins of the neck ([illegible] gram shows the large [illegible] If the heart is viewe[illegible] right auricle is in front, to the observer's left, and its pulsation is presystolic and precedes that of the left ventricle lying behind and to the observer's right (9) The *angiocardiogram* shows that the auricles fill together (10) [illegible] ventricle not at all [illegible] Sometimes they are

[illegible] and indicates left ventricular hypertrophy The combination of this type of curve and a cyanotic lesion is diagnostic The auricular waves (P) tend to be of high voltage

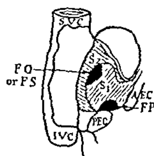
The *cardiac catheter* fails to enter the right ventricle, but may pass into the left auricle easily This does not help much in the diagnosis The oxygen saturation of the blood in the right auricle may be but little less than that of the arterial in some cases; in others there is considerable arterio-venous oxygen difference

The Blalock operation would be worth while if the lungs seem to be ischæmic in the skiagram The mortality is higher than in other cyanotic lesions If the lungs are well supplied, it would be dangerous to increase the flow

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ATRIAL SEPTAL DEFECT

Development. Formation of the atrial septum begins in the *fourth or fifth week of fœtal life, and is complete, apart from the* foramen ovale, by the eighth week. The partition of the auricles is first brought about by the growth of the septum primum This grows in the form of a crescent, with its concavity downwards. (Caudad.) The opening in its lower portion is the ostium primum. This aperture closes, meanwhile a second opening forms higher up in the septum primum, the foramen secundum. On the right-hand side of the septum primum there now forms the septum secundum,



S.V.C	*Superior vena cava*
I V C.	*Inferior vena cava.*
F P	*Foramen primum.*
F.O.	*Foramen ovale or secundum*
S_1	*Septum primum*
S_2	*Septum secundum*
A.E.C.	*Anterior endocardial cushion*
P.E C.	*Posterior endocardial cushion*

FIG. 14 Formation of *interatrial septum.* (After Walmsley)

thicker than the first septum An aperture left by this septum is the foramen ovale with its thick rim, the annulus ovalis (Fig. 14) Blood can still pass from right to left through this valvular opening It could not pass from left to right because of the valvular character of the opening In some 16% of cases the opening does not completely close after birth and can still let pass a probe from right to left. This apparently complex process of growth is necessary in order to provide a shunt from right to left in fœtal life, which can be disused at birth, and yet later prevent a left to right shunt when the pressure in the left auricle rises after birth *(1)*

Types of defect. Three types of atrial septal defect may be of pathological importance.

Persistent ostium primum With this the anterior cusp of the mitral valve may be cleft, leading to mitral incompetence

Ostium secundum defect Here this opening coincides with the foramen ovale.

Patent foramen ovale Slit-like openings are not included here

In some instances the whole septum is wanting. This classification (1) may be followed.

1. Normal septum, ostia overlapped. Foramen ovale sealed. Foramen ovale unsealed (valvular)
2. Abnormal septum, ostia not overlapped

   Ostium primum

      Alone
      With ostium secundum.
      With valvular foramen ovale

   Ostium secundum

Incidence. This is a common congenital defect It occurs as a sole lesion in 7–25% of cases (2, 3) but figures are variable and the modern methods of investigation may cause them to change Females are more affected than males, perhaps twice as many. Other lesions are found with atrial septal defect, particularly pulmonary stenosis, and abnormal pulmonary veins. Physical growth may be stunted and frail (4).

Morbid physiology and anatomy. There is a hole between the auricles anything from 1–3 cm across There is usually a shunt of blood from the left auricle to the right The flow may amount to 30 or 60% of the output from the right ventricle (5) Exertion may reverse the shunt by raising the pressure in the right auricle The usual flow from left to right may be due to the pressure in the left auricle being a little higher than the right, but the difference is really small (6) In the upright posture the left auricle lies at a slightly higher level than the right (7), but this may not be important The defect varies in size It has been suggested that when its area is more than 2 sq. cm there is no significant difference in the pressures on the two sides there is in actual fact just one common atrium (28, 33) While in some cases the causes mentioned above may operate, when there is no important difference in pressure, the flow from left to right may depend on the different distensibility of the two ventricles or to resistance in their circulations (13) The stroke volume of the right ventricle is greater when the pressure [illegible]
blood fron
the right v
[illegible]

[illegible] reach
[illegible] a minute, three or four times the normal at rest.

Despite this huge flow the pulmonary circulation can accommodate it without rise in pressure as a rule (*43*). The right auricle will enlarge. The venous waves show a large "V" wave which can be recognised by its coincidence with the second sound of the heart (*8*). If there is pulmonary hypertension the "a" wave of the jugular phlebogram may become large (*6*, *9*).

The increase in the size of the right auricle can be associated with P waves of high voltage. Increase in the P-R interval (heart block) is quite common but these points vary much (*10*, *11*, *12*). As the years go on the enlargement of the right ventricle may become extreme There is both dilatation and hypertrophy Clinically there is a heaving impulse just to the left of the sternum over the right ventricle. Dullness on percussion may extend to the right of the sternum The beat at the actual apex is tapping. The first sound is loud in the tricuspid area (*27*). A murmur due to auricular systole may cause a tricuspid diastolic murmur (*27*) Over the pulmonary artery a pulsation may be palpable, in fact, almost a thrill if the patient is thin The closure of the pulmonary valves may be felt A systolic murmur is usually audible here, hollow sounding and of low pitch The cause of this murmur, a true ejection murmur, is the increased flow of blood through the dilated pulmonary artery which is also nearer the surface of the body than usual (*27*), not the atrial septal defect. The second sound in the pulmonary area is split The pulmonary component is the second, for the right ventricle is overfilled and empties more slowly (*47*) The splitting is wide and fixed The pulmonary component is louder than the aortic (*9*) If there is pulmonary hypertension the pulmonary element becomes very loud indeed If the flow decreases it may become soft (*27*). In half of the cases there is the Graham Steell murmur of pulmonary incompetence (*9*, *12*) Sometimes there is a functional mid-diastolic murmur near the lower sternum due to increased flow of blood through the tricuspid valve

ELECTROCARDIOGRAM In some 80% of cases this shows more or less delayed activation of the surface of the right ventricle, the duration of QRS being prolonged (Partial or complete right bundle branch block) (*9*, *13*, *14*, *33*) In V1 of the precordial leads there may be a conspicuous R wave coming rather late, seen also in V2 and V3. VR has a similar appearance The T wave over the right ventricle is usually negative. Over the left ventricle (V6) the intrinsic deflection is earlier (Fig 15) The unipolar limb leads suggest a vertical position The effect of the increased filling of the right side of the heart is to produce dilatation and hypertrophy,

as stated In France enlargement due to dilatation such as this is sometimes called "hypertrophie de surcharge" and is linked with the cardiogram commonly found in these cases. This is in contrast to the curve of "hypertrophie de barrage" found in pulmonary stenosis (*13*) If the pressure rises, the cardiogram may alter in type and become more abnormal than before; the curve may become more that of right ventricular hypertrophy (*34*) After operation there may be less abnormality (*14*) The vectorgram does [illegible]
b [illegible]
g [illegible]
true right bundle branch block the appendix of the horizontal loop is to the right running anti-clockwise In hypertrophy (RSR′) the loop runs clockwise to the right and later to the left (*44*) The RSR′ pattern may be due to delay in the activation in the basal parts of the right ventricle There may be some relation between the pattern of RSR′ in V1 and the volume of the fluid, the pressure being normal The large P waves in V1 and V2 may also be related to the flow (*45*) The association of the RSR′ pattern in V1 and left axis deviation or left ventricular predominance has been found with a persistent ostium primum with a cleft mitral valve (*46*) RSR′ alone is seen in some two-thirds of cases, and means hypertrophy of the right ventricle Auricular fibrillation or flutter are not uncommon in the later stages The P-R interval is often prolonged before the auricle fails

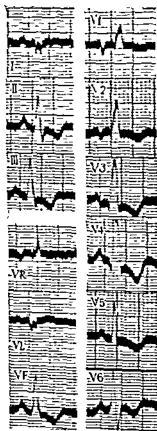


FIG 15 Lutembacher's Disease Note delayed R in V1, V2, V3, V4, V5 Negative T waves in precordial leads Vertical heart

CARDIAC CATHETERISATION The catheter may pass through the septal defect into the left atrium, and so into a pulmonary vein It may occasionally pass into the left ventricle The blood in the right atrium may show a saturation with oxygen of 80 or 90%, in

contrast with that from the superior or inferior vena cava of some 70%. This depends on the degree of *mixture by left to right flow*. Abnormal saturation with oxygen may be due to anomalous pulmonary veins. It is not uncommon for a vein from the right lung to drain into the right atrium when there is an atrial septal defect. In fact pulmonary veins draining into the right atrium or great veins have the same effect as a patent atrial septum The pressure in the right auricle and ventricle is not raised in the large majority of cases (*9*, *10*). In children the pressure is usually low. The higher pressures tend to be found in older patients (*19*, *20*, *21*)

Pulmonary hypertension is an important complication in these cases. The pressure in the pulmonary artery may reach 60–80 mm. Hg (*13*). There does not seem to be any close relationship between the volume of the pulmonary flow and the level of the pressure A moderate rise may be hyperkinetic and due to a large flow without increased resistance (*43*) If the pulmonary bed is normal the increased flow is easily accommodated (*43*) Quite a small increase in flow may be associated with a rise in pressure if there is increased resistance. The rise in pressure is due to obstruction in the pulmonary arterioles (*18*). There is medial hyperplasia, intimal proliferation (*42*), and often thrombosis, so that the vascular resistance may become very high (*26*) If the pressure is normal, normal vessels are found (*42*).

Radiology The remarkable systolic pulsation is seen in the large pulmonary artery and its branches. This variation in the shadow is better seen in the right lung field at the edge of the heart. This abnormal pulsation is particularly related to the increase in flow, not to any rise in pressure (*15*) But pulmonary hypertension *still further enhances the pulsation if it is already present*, yet it will not do so alone. The enlargement of the right auricle and ventricle is confirmed, particularly in the oblique view from the left (*9*) The angiocardiogram may show that both atria fill together, in fact all four chambers of the heart may be depicted at once

Course and prognosis. REVERSAL OF THE SHUNT Cyanosis tends to appear late A mild degree of cyanosis may be due to some minor degree of random mixing in what in fact amounts to a common atrium (*26*) It may appear transitorily after severe exercise, or after performing Valsalva's experiment when the inflow of venous blood into the right auricle rises This may be detected by an oximeter on the lobe of the ear (*36*) Severe cyanosis is due to a fall in the output of the right ventricle This failure of the right ventricle is mainly due to an increase in the resistance of the pulmonary



A. Early phase



B Late phase

Fig 16 Atrial septal defect

circulation, and the resultant pulmonary hypertension There may be tricuspid reflux Actually the diastolic pressure is not raised in the right ventricle when it fails. The output falls, and this leads to the shunt of blood from right atrium to left (*26*). The thrill and murmur in the pulmonary area may decrease (*14*) Towards middle life the heart may become enormous having remained unaltered in size for many years (*33*). Auricular fibrillation and flutter are not infrequent It is the only common congenital defect with which they are associated. A very fast rate may cause syncope, and so may sinus standstill (*49*). Infection of the opening is most unlikely to occur. Although considerable enlargement may be seen, yet *many patients keep fairly well for years, usually past 30 or 35* Heart failure tends to come on in middle life, and the cyanosis may be severe (*33*) Some patients, however, reach old age (*37*). The clinical picture in the later stages is very different from that of early years *It would appear that the course of the case depends very* much on the development of pulmonary hypertension and the associated vascular obstruction in the pulmonary arterioles In some instances it has been noted that failure of the left ventricle may come on. The diastolic pressure in that chamber is raised, but the fall in output is small (*26*). In children growth is retarded, chest infections are common. The same cardiac findings are found as in adolescence or young adults (*41*)

Associated lesions The combination of pulmonary stenosis and atrial septal defect is considered under the pulmonary valve lesions (p. 43) It is met with in some 10% of all cases of A S D (*33*) The abnormal pulmonary and great veins are mentioned elsewhere (p. 88), the subject also arises under transposition (p 25)

MITRAL STENOSIS (Lutembacher 1916, Maude Abbot 1915) This combination is much less common than formerly was supposed *when autopsy findings are considered (22) It is almost entirely* confined to women. The murmur and thrill of mitral stenosis may be detectable but they never reach the intensity of pure mitral stenosis, because the septal defect acts as a safety valve The *abnormality of the mitral valve may be congenital or acquired* the latter is more likely

PERSISTENT OSTIUM PRIMUM Occasionally there is mitral incompetence and the left ventricle may then be enlarged (*28*) A loud systolic murmur, *mitral or tricuspid, is heard in persistent* ostium primum, and has been called false Lutembacher disease The defects of the mitral valve are likely to be associated with persistent ostium primum. The diagnosis is *important in view of*

the surgical difficulty in closing it. The left to right shunt is large, there may be mitral or tricuspid reflux. The left axis deviation in the ECG refers to the mitral reflux which goes with the ostium primum There may be a ventricular septal defect. Gross enlargement of the heart may develop in childhood (48). The following classification may help to make clear this rather complex situation (51)

DEFECTS OF THE ENDOCARDIAL CUSHIONS In the sixth week the dorsal and ventral cushions of the auriculo-ventricular canal may fail to fuse (1) In the mildest type there is a persistent ostium primum and a bifid anterior cusp to the mitral valve (2). More severe is an associated deformity of the septal cusp of the tricuspid valve (3) The auriculo-ventricular canal persists At the top there is persistent ostium primum, and below is a ventricular septal defect The dominant hæmodynamics are those of the A S D., but there may be a shunt from left to right at the level of the ventricles The left ventricle will probably be as much enlarged as the right The recognition of an incompetent auriculo-ventricular valve, mitral as a rule, helps to distinguish the straightforward A S D, which is becoming a practical surgical problem, from the much more difficult defect of the endocardial cushions (51) The association of pulmonary stenosis must be remembered The diastolic *murmur* at the apex in some instances is due to the greatly increased flow through the mitral valve which is not stenosed Perhaps one-fifth of all cases have this murmur (22) An unusual type of *shunt* resembling an atrial septal defect has been noted at autopsy with a ventricular septal defect and an abnormal tricuspid valve allowing blood to enter the right atrium (23)

Treatment. Several methods are under trial for curing this defect The mortality is falling Technical difficulties are great, for the defects vary in size and site It is suggested that closure might be attempted when the heart is beginning to fail (22) But this might be too late, for irreversible pulmonary hyperten-
have been established, and
shunt is reversed, which woul
suggestion depends on the volume of the pulmonary flow, if it were thrice the normal operation would be indicated (20). Probably all cases should be operated on if they have persistent ostium secundum A *persistent ostium primum* however is the most difficult to close and mortality
one in ten cases nay occur in
hypertension is pulmonary
systolic murmur of

mitral or tricuspid reflux; the cardiogram may show left ventricular predominance; there may be complete heart block; left to right shunts are found between auricles and ventricles (*38*). In some hands the "atrial well" technique of Gross is successful, with some 4% mortality (*29*). Hypothermia with a dry right heart is now generally used here, but time is short, and there is some risk of ventricular fibrillation when the temperature falls too low, below 31°C With the left forefinger exploring the atrium and guiding the needle direct suture of the defect is fairly easy. In this way most of the aperture of an ostium primum can be closed (*30*). For the ostium primum an extra-corporeal circulation is needed (*50*), but is not always satisfactory (*31*) The difficulties lie in the variable anatomical conditions, but valuable advances are being made and no doubt will go further. Once the closure has been done the results are good and things return to normal (*40*) Pressure in the left auricle is not raised by closure of the defect The pressure in the pulmonary artery and right ventricle falls if it was raised (*40*), the heart diminishes in size (*38*) The improvement is rapid and dramatic (*50*). There is less dyspnœa, for the lungs are less stiff (*19*). Any abnormal pulmonary veins can be dealt with at the time of operation

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51 Campbell, M, Missen, G A K 1957 *Brit Heart J* 19, 403

ABNORMAL SEMILUNAR VALVES

The aortic and pulmonary valves are developed from four

... two may persist only in the aorta, giving a bicuspid aortic valve (Fig 18) or a supernumerary cushion or two may produce extra pulmonary cusps (Fig 19) Spitzer's explanation for the bicuspid aortic valve, where there is transposition, is that it represents the primitive reptilian right aorta which has two valves Bicuspid aortic valves are closely associated with abnormalities of the aortic arch ...

... (1).

Bicuspid pulmonary valves occur in infundibular stenosis and in the Tetralogy. They are not liable to infection or to calcification Even when there are four or five pulmonary cusps they may function



FIG. 17 Formation of the semilunar valves
(After J. W. Brown)

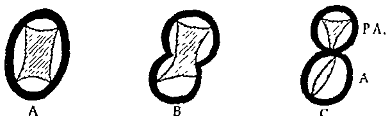


FIG. 18 Formation of the bicuspid aortic valves
(After J. W Brown)



FIG 19 Formation of supernumerary cusps in pulmonary artery
(After J. W Brown)

quite well, but three are probably the most efficient A supernumerary cusp, or cusps, might be suspected when there is unexplained pulmonary incompetence (Fig. 19)

It is suggested that rheumatic infection may be responsible for those cases where no other congenital defect is present The commissural lesion in acute rheumatism may cause fusion of the adjacent

cusps. The raphe in the bicuspid valve contains collagenous and not elastic tissue, and there are other signs of past inflammation. These are the lesions peculiarly liable to infection and calcification.

The defect in bicuspid aortic valves was shown to be associated with an abnormal position of the elastic tissue in relation to the annulus fibrosus where it lay superficially at the raphe which represents the abortive commissure The presence of a ridge on the wall of the aorta at the commissure, slightly involving the sinus and composed of elastic tissue, may be characteristic of the congenital defect

Probably both types in time tend to become calcified and infected. Distinction can only be made by histological examination and this may not be easy owing to gross change due to the calcification The senile fibro-calcareous aortic stenosis, often seen in old men, may be the final result of these lesions in many cases.

The possibility of surgical treatment of the stenosis arising from these defects is considered on page 47.

1 *Franchesi, J et al* 1954 *Amer Heart J* 47, 664

ABNORMALITIES OF THE AORTIC ARCH

Of the primitive six pairs of aortic arches, the first three cephalic pairs disappear The fourth arch on the left side becomes *the arch* of the aorta, on the right side it forms the innominate, and part of the right subclavian arteries The fifth arches disappear, the right sixth arch gives rise to the pulmonary artery, and the left to the ductus arteriosus

Possibly through stenosis or some other cause, the fourth left arch may disappear, wholly or in part, and the fourth right arch persist instead, as it does in birds Perhaps this stenosis leads to coarctation if it occurs after the right arch has disappeared Occasionally, both arches persist complete

Three types of abnormality may be distinguished —

1 Right [illegible]
2
3

The degree of persistence of the left arch distinguishes these three

1 The aortic [illegible]

Bicuspid pulmonary valves occur in infundibular stenosis and in *the Tetralogy. They are not liable to infection* or *to calcification* Even when there are four or five pulmonary cusps they may function



FIG. 17 Formation of the semilunar valves (After J W Brown)

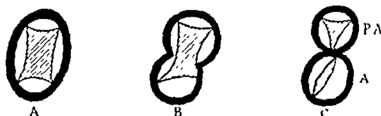


FIG. 18 Formation of the bicuspid aortic valves (After J W Brown)

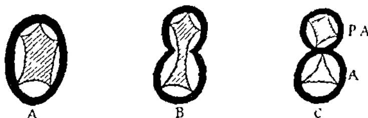


FIG 19. Formation of supernumerary cusps in pulmonary artery. (After J. W Brown)

quite well, but three are probably the most efficient A supernumerary cusp, or cusps, might be suspected when there is unexplained pulmonary incompetence (Fig 19)

It is suggested *that rheumatic infection may be responsible for* those cases where no other congenital defect is present The commissural lesion in acute rheumatism may cause fusion of the adjacent

X-ray examination shows that there is usually no aortic knob on the left, the aortic arch projects to the right as a knob or band The persistent left root of the left arch may appear as a small knob on the left, thus two knobs may be seen. Barium in the œsophagus shows the relations very well The ductus arises from [illegible] and completes the vascular ring. The trachea is [illegible]

3 There may be a double arch The [illegible] œsophagus to form the descending aorta Each arch gives off its appropriate branches The left is anterior and smaller This is very rare

The diagnosis is purely radiological

PHYSICAL SIGNS are suggestive but not definite. There may be dullness to the right of the sternum. The aortic second sound is heard high up There may be some pulsation over the dull area There may be a tracheal tug These all suggest also aneurysm Paralysis of the vocal chords may occur

SYMPTOMS These may refer to the branches or œsophagus. The ligamentum arteriosum springing from a right aortic arch may cause strangling in infancy, with dysphagia, stridor and wheezing, the head being held back Both these defects may be relieved by operation In the first the ligament can be cut, and in the second the smaller arch divided (2)

ABERRANT MAIN BRANCHES There may be an aberrant right subclavian artery running from the descending aorta, which may pass behind the œsophagus and indent it Indentation will appear in the shadow of the barium swallow This artery may cause no symptoms It may occur with coarctation If it leads to dysphagia it can be divided

An anomalous innominate and left carotid artery may occur and cause pressure on the trachea They can be pulled out of the way (2) The dysphagia caused by these anomalies has long had the odd epithet "lusoria," but it is real enough

1 Mann, W 1947 *Guy's Hosp Rep* 96, 186
2 Gross, R E 1955 *Circulation*, 11, 124.

COARCTATION OF THE AORTA

The earliest classification by Bonnett (1903) recognised two types, the infantile which was a diffuse narrowing of the aortic isthmus,

behind the œsophagus to leave the thorax by the usual opening (Fig. 20A). Alternatively, *the aorta may persist on the right side* throughout its thoracic course.

The left subclavian artery (representing the fourth left arch) may rise from the aortic arch and pass to the left in front of the trachea (Fig 20B). It is then a homologue of the normal aorta (*1*) The ductus



FIG 20A Right aortic arch

R S C Right subclavian artery
L S.C *Left subclavian artery*
P A Pulmonary artery
D A. Ductus arteriosus

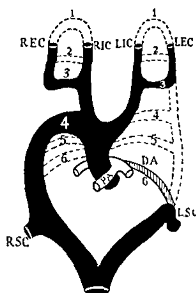


FIG 20B Right aortic arch with persistent left root.

L S C *Left subclavian artery*

(After J W Brown)

arises from it, or from the aorta. Thus a vascular ring is formed round the trachea and œsophagus. *The œsophagus is not pushed* forward. Instead the left subclavian artery may pass behind the œsophagus. Its impression on the œsophagus filled with barium gives the diagnosis

[illegible]

structures forward The ductus pulls the diverticulum to the *behind the œsophagus so that the œsophagus is pushed forward and* to the left.

coarctation the aorta is often thin walled and dilated and there may be aneurysms

[illegible] common in older valves are often They appear to

be abnormal in some 40% of cases

Congenital defects in the cerebral arteries are common, giving rise to aneurysms, which may burst and cause subarachnoid hæmorrhage in one-tenth of cases (5) More widespread abnormalities may be found in other parts, particularly in the abdominal [illegible]

There is a raised blood pressure in most cases But not always in children (2). This rise in pressure depends on ventricular systolic discharge and the capacity of the aorta and the distensibility of its wall Both are variable (3) At least half the lumen must be lost (4) It is clear that the obstruction is in some way responsible for the high pressure, and this may be associated with increased tone in the arterioles of the upper part of the body It has been shown that there is actually a decrease in the renal blood flow, but a normal rate of glomerular filtration But the modern view is that no cause arises in the kidneys (4)

The blood pressure may be very different in the arms This is due to anomalies in the great vessels, a weaker right radial pulse may be due to an abnormal origin of the right subclavian artery, or to stenosis at its origin A weaker left radial pulse may be due to stenosis of the left subclavian artery, or to a coarctation proximal to the origin of this vessel, which may cause enlargement of the right arm and shoulder There is usually hypertrophy of the left ventricle

THE [illegible] ant features of the is pulsating arteries There are scapular [illegible] and internal mammary anastomoses, also intercostal and spinal The collateral circulation can be demonstrated in the back when the patient stoops forward Pulsating vessels can be seen and felt and murmurs heard, systolic and diastolic in time (9)

The [illegible] to th[illegible] bord[illegible] The loops are conspicuous

and the adult which was a sudden constriction distal to the mouth of the left subclavian, near the origin of the ductus arteriosus Three commoner types may be defined (W. Evans).

1. Stenosis of arch, hypoplasia proximal to stenosis, ductus patent.
2. Stenosis of arch, hypertrophy proximal to stenosis, ductus closed.
3. Atresia of arch, hypertrophy proximal to stenosis, ductus closed.

These account for most of the adult cases.

Pathogenesis. The adult type of coarctation has never been found before or at birth. It may be that the process of the closing of

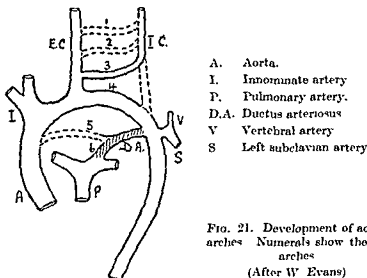


FIG. 21. Development of aortic arches Numerals show the six arches
(After W Evans)

the ductus involves the wall of the aorta, and there is some histological evidence for this. But sometimes the constriction is not so near, and also the ductus may remain open above or below it It is significant that the defect arises at the junction of the fourth and *sixth primitive arches.*

Morbid anatomy. The proximal part of the aorta may be hypoplastic, but is more often dilated

At the site of coarctation the aorta may be completely closed as by a diaphragm, or there may be a small central hole of varying size. Sometimes the constriction is tapering and several centimetres long, sometimes in the form of an hour glass Below the

in young children the prognosis here is bad, unless operation is done (26) If the constriction is proximal to the left subclavian there are no anastomoses on the left side of the body (Figs 22 and 23).

Clinical features. Males are more often affected than females. Symptoms often do not appear for years. Those associated with the high pressure are headache, giddiness, throbbing in the head, epistaxis Aortic incompetence may result from the stretching of the aorta The increased vascularity may lead to hyperthyroidism. Palpitation may be troublesome.

The upper part of the body tends to be well developed, with high complexion and warm moist hands.

There is more or less hypertrophy of the left ventricle; a diastolic murmur has been heard at the apex (24). It has been suggested that this is due to the lumen of the left ventricle becoming small from the thickening of the wall (concentric hypertrophy), and so causing stenosis (23) In early infancy coarctation is a serious cause of death, particularly with a ductus patent below the constriction (29)

Much depends on the degree of coarctation, the rise in blood pressure and the associated lesions, if any Mild types, and they are perhaps commoner than supposed, may be missed clinically A systolic murmur and thrill towards the base of the heart, and near the left clavicle or scapula, or an unexpected high blood pressure may draw attention ...

rtery settles

in the left

clavian artery may be seen running upwards from the aorta. The œsophagus may, when filled with barium, show two indentations, one above and *one below* the constriction Pulsation of the aorta below the coarctation is reduced The angiocardiogram may show the constriction and delayed filling of the aorta below it, but the contrast medium is apt to be diluted at this stage Aortography is the best method. A catheter is introduced through the left radial artery as far as the coarctation and then withdrawn a little, and 25 ml of 70% diodrast injected (2) (Fig 24)

THE ...

ventricl

is in fa

the pre ... the left ventricle will be found

If the ductus arteriosus opens proximal to the coarctation there may

between fixed points in the arteries, at the angles of the ribs or further round, and are curiously symmetrical It is supposed that pressure by the loops may cause thoracic pain in some cases The notches do not appear in very young children as a rule, in fact they are rare under the age of six years (*2*). Aneurysms may form in these large arteries (*24*)

Distal to the obstruction. The relatively poor blood supply to the legs and feet makes those parts cold and pale, patients complain of weakness of the legs on walking and intermittent claudication.



FIG 22. Coarctation ductus closed

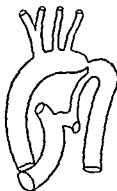


FIG 23. Coarctation ductus open

The obstruction leads to a lower systolic blood pressure in the legs than in the arms, and to weakening and retardation of the pulse in the legs: a delay of 0 03 sec. has been noted Pulsation may be hardly palpable in the abdominal aorta and in the femorals While the systolic pressure tends to be lower than normal, the direct measurement of the diastolic pressure is as high or higher than normal The damping of the pulse wave makes it difficult to hear the Korotkov sounds. The low pulse pressure makes it difficult to feel the pulse wave However, the mean arterial pressure in the leg is but little different from that in the arms It has been noted that there is a thickening of the arterioles below the coarctation, intimal and medial, which may be associated with the raised diastolic pressure (*11*).

The *ductus arteriosus* is patent when this structure is below the stricture. Some 7% of all cases of coarctation have a patent ductus arteriosus (*25*) Usually the ductus is proximal, but may be opposite or distal If below, there is cyanosis of the lower part of the body

Operation. Since Crafoord first remedied the defect in 1944, a considerable amount of surgical experience has accumulated. The selection of the time to operate will be governed by various reasons. If the blood pressure is becoming higher and the left ventricle showing signs of overstrain, by considerable enlargement and abnormalities in the electrocardiogram such as negative T waves, it should be advisable to reduce the load. If the patient is a child, growth may theoretically leave the site of the operation relatively too small, particularly if a graft has been used But in fact aortography and experiment seem to show this is not the case (28). In adult life the presence of degeneration in the aorta adds difficulties, and irreversible defects in the left ventricle may have developed Probably the best time is from 10 to 20 years (18), or even younger, from 5 to 16 years (28) Thoracic operations of this magnitude are better tolerated when young Hypertension is usually not so severe at earlier ages, the aorta is healthy

Nowadays the immediate results are usually good, perhaps 90%, and mortality low, under 5% (24). But it rises a great deal in middle life The technical difficulties may be considerable, and depend on the length and extent of the constriction This can sometimes be discovered to some extent by the angiocardiogram, the aorta being injected (2), but the actual situation can only be finally appreciated at the time of operation Grafts are often needed, particularly in adults, and one should always be available in case it is wanted, particularly if aneurysms are present below the isthmus (20) The blood pressure may be lowered temporarily by Arfonad

I.

bec

the. the pressure falls to a normal level, but not perhaps for several weeks or later (22) After 5–7 years in one series the femoral and brachial pressures were within normal ranges The diastolic in the femoral tends to stay below the brachial (22). In another series the brachial diastolic and systolic pressures fell, but still remained above the average for the age (24) This result of course depends on the new lumen being adequate, that is to say at least three-quarters of the normal (20)

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2 Shapiro M J 1949 *Amer Heart J* 37, 1045
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5 Reifenstein, G H et al 1947, *Amer Heart J* 33, 146

be preponderance of the right ventricle (*8*) resulting from the shunt into the pulmonary circulation.

Course and prognosis. Heart failure may end a fifth of all cases (*5*), as a result of high pressure, perhaps aided by aortic reflux; but many escape it. The aorta may rupture in about this number; cerebral hæmorrhage from a congenital aneurysm may kill one-third Infection of the bicuspid aortic valves or of the area of coarctation



FIG 24 Coarctation of aorta.

is not uncommon Perhaps one-quarter live out a normal span of life and die of something else. Thrombosis in an aneurysm at the site of a partly occluded ductus may occur.

Patients not uncommonly reach old age without trouble if they pass the thirtieth year, even with very high pressures such as 250/150 or more (*12*) Sudden strain is particularly dangerous (*13*). If symptoms occur early, death is likely to occur soon after the age of thirty (*14*). But the average do not pass middle age.

PREGNANCY. It is generally agreed that this introduces special dangers. There is a risk to both mother and fœtus (*15*) While some may come through well, probably about half are the worse for it (*16*) Cæsarean section at term is suggested, and resection of the coarctation later (*15*). Rupture of the aorta seems not uncommon here But a patient previously well may sink into fatal failure (*17*) Each case must be judged on its merits, but the dangers may be greater than appear at first

pulmonary artery to aorta for the first few hours; it is gone by the third day (3)

FAILURE TO CLOSE The reason for this is not understood. An abnormal angle with the aorta, or particularly thin walls have been suggested The neuromuscular closure may depend on the presence of oxygen in the blood, and this depends on breathing, so atelectasis of the lungs might play a part. There is a not uncommon association with coarctation of the aorta Maternal rubella has nothing to do with it The bore of the ductus varies much—from 2–5 mm; also its length There may be a direct anastomosis in older patients. The wall may be thin with aneurysmal dilatation The channel may join the pulmonary artery in either branch or at the bifurcation. There may be a slight familial incidence Girls provide some 70% of cases It may be commoner among those born in the latter part of the year (4) It occurs more often in the first born.

Clinical diagnosis. In over one-third of newly born babies the characteristic ductus murmur may be heard for a time. Possibly mild asphyxia may cause some contraction in the pulmonary vessels and increased disturbance in the pulmonary artery (36). Later in the first year of life the typical murmur may be absent; only a systolic murmur may be audible (2) Sometimes no murmur is heard at this age (6) On the other hand the characteristic murmur of the lesion may be heard already (5) The sound described by G A Gibson in 1900, "a continuous rushing murmur beginning *after* the first sound, and continuing almost to the next first sound," reaching its loudest about the second, is audible The quality varies, sometimes it is hollow, usually, in a child, it can be heard at the back of the left shoulder usually it is loudest just below the left clavicle. In adults the murmur may be difficult to hear, particularly the diastolic part Rising pressure in the pulmonary artery affects the flow and murmur Valsalva's experiment may diminish this portion Other murmurs may mimic the true Gibson murmur. They are an aortico-pulmonary artery fistula, a communication between the aorta and right ventricle, an aneurysm of the sinus of Valsalva, a fistula between a coronary artery and the right ventricle, or a coronary arterio-venous fistula (39), very large bronchial or internal mammary arteries, arterio-venous aneurysm of the lung, and some very vascular tumours, and occasionally lesions of the aortic valves The large left ventricle gives a hint here (38) The closure of the pulmonary valves is loud and often palpable The second sound may be split The splitting may be "reversed", the pulmonary element coming first (35) Pulsation may be palpable

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28. d'Abreu, A. L. 1958. *Brit. med J.* 1, 957.
29 Bonham-Carter, R. E. 1958. *Brit. Heart J.* 20, 261.
30 Hayward, G. 1958. *Brit. Heart J.* 20, 262.

PATENT DUCTUS ARTERIOSUS

During fœtal life, before the use of the lungs calls for a full pulmonary circulation, the blood passing into the pulmonary artery is carried into the aorta by the ductus arteriosus.

NORMAL CLOSURE. *Closure of the ductus takes place in two phases* The first is physiological, and due to contraction of the muscular coat of the ductus; the second is anatomical and is marked by a process of obliteration, which starts at the pulmonary end of the duct and spreads along it *(1)* In stillborn babies the ductus is uncontracted Breathing causes constriction. The contracted ductus tapers at the aortic end, and is stiffer and less flexible *(37)*. The rate at which the proliferation of the intima is carried out varies, probably about half are closed in a month; most are closed by the second year *(2)*. It has been suggested that kinking of the canal, or traction on it may initiate the preliminary muscular spasm. It has been shown that after birth for a few hours the blood in the feet is significantly less well saturated with oxygen than that in the hand, about 5–10%. This suggests that there may be a shunt from

All these features vary much; this makes them unreliable; the extent of the shunt and the time it has been there cause many differences The size of the ductus is hard to gauge. Perhaps the degree of pulsation in the pulmonary vessels is most important. Some stress the presence of a very low diastolic pressure and the diastolic murmur at the apex (*7*, *9*). This is probably due to the greatly increased flow from the left auricle into the left ventricle, which is dilated, the mitral valve showing "relative" stenosis (*10*).

Hæmodynamics. There is a higher pressure in the aorta than the pulmonary artery as a rule, so that flow is from the aorta into the pulmonary artery, unless the pulmonary pressure is higher than the aortic. It may be that 20–60% or more of the output *from the left ventricle* passes through the ductus into the pulmonary artery (*11*) The volume of the flow will depend on the difference in pressures at either end of the ductus, and on its size A large short ductus gives a large pulmonary flow and is likely to be associated with raised pulmonary pressure (*31*) The output into the pulmonary circulation may be double that into the peripheral (*12*) The ductus flow may reach over 7 litres per minute (*11*). *To make good this loss* into the pulmonary circulation the output of the left ventricle must be proportionately increased The oxygen content of the blood in the pulmonary artery on cardiac catheterisation may be over 80% (*7*) The cardiac catheter may often pass through the ductus into the aorta

There is a tendency for the pressure in the pulmonary artery to rise, due at first to the increased flow Later the pulmonary peripheral resistance may be increased, when the pressure in the main pulmonary artery is low then the resistance is, of course, low too, and vice versa, unless the rise is hyperkinetic (*7*) The result of the increased inflow causes the pulmonary artery to enlarge, and the valves may become incompetent (*12*).

ASSOCIATED LESIONS In the majority of cases that survive there are no other defects

Pulmonary stenosis may occur The characteristic harsh murmur may be distinguished lower down than that of the ductus The ductus should be closed, the pulmonary valve can be dealt with after assessment with cardiac catheter, if the right ventricular pressure exceeds 100 mm Hg, or the cardiogram shows right ventricular strain. Actually the curves vary, there may be right bundle block pattern Left ventricular hypertrophy may also be seen The pulmonary vessels will be full (*41*).

With *aortic stenosis* the separate murmur can be heard, there may

over the large pulmonary artery and some dullness on percussion may be elicited There may be a thrill if the chest wall is thin. The beat of the heart is as a rule vigorous or hyperdynamic. A soft "functional" diastolic murmur may be heard at the apex due to increased mitral inflow (7). A "snap" in mid-diastole may also be audible, and a soft systolic at the apex. These disappear after operation (35). The pulse is full and bounding, of the Corrigan type,

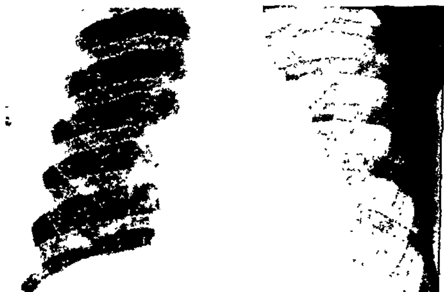


FIG 25. Patent ductus arteriosus

with lively pulsation of the arteries in the neck (7). The mean systolic pressure is usually higher, and the mean diastolic lower than usual The test of the effect of exercise is not really helpful, the fall in the diastolic pressure must be at least 15 mm of mercury (8) In any case in children the pressures are apt to be very unstable

RADIOLOGICAL FINDINGS. The most important is dilatation of the pulmonary artery. The pulmonary branches tend to be full and to pulsate freely. The pulsation of the left ventricle may be increased and the chamber enlarged The left auricle may be dilated (Fig 25)

CARDIOGRAM. This is usually normal in the first part of life Occasionally there is predominance of the left ventricle Right-sided predominance would suggest a complication such as transposition or pulmonary hypertension

hypertrophy of the right ventricle and right axis deviation is seen in the cardiogram (*18, 20*)

REVERSAL OF THE SHUNT. When the shunt is reversed there is cyanosis, "differential cyanosis." The face and arms are less affected than the feet. This may be present at birth (*19*), or appear later (*18*) The arteriolar resistance is raised. The *murmur* may be deceptive. In some cases there is no characteristic Gibson murmur (*20, 21*). Only a systolic murmur may be audible, due to the flow from pulmonary artery to aorta (*22*), or the pulmonary valves may be incompetent, and only a loud diastolic murmur, even with a thrill, be noted (*17*) If the pressure be raised in the pulmonary artery the flow from the aorta will only be in systole, and so no diastolic component will be heard The pulmonary hypertension may appear as a gradual rise *pari passu* with the increased flow, but in some cases it seems to be present from the start (*23*) On the other hand, some observers do not consider that the increase in flow

[illegible]

considerable fall in the pulmonary pressure.

Course and prognosis. Although some patients may survive past the age of fifty, it is rare to meet them above the age of forty Two have been recorded over seventy and one over eighty (*33*) There was no thickening of the arterioles in the lungs (*25*) In about half the patients heart failure comes on, and in a quarter bacterial infection of the ductus develops The infection starts at the pulmonary end of the ductus, and may arise where the stream impinges on the wall of the pulmonary artery opposite From here the infection may spread down to the valves In a very few ...

[illegible]

... from the aorta (*28*)

The Gibson murmur may be simulated by those due to other lesions as already noted such as large ...

also be an early aortic diastolic murmur. The systolic murmur has the characteristic "diamond pattern" in the phonocardiogram *(40)* and its quality is different to the ear from that of the ductus. The carotid pulse tracing shows delayed ejection *(40)*.

Ventricular septal defect may be suspected from the presence of the murmur, but diagnosis will be difficult and confirmation by catheter needed. It would seem to be a serious combination. Certainly the ductus should be closed.

Coarctation may cause interesting results. What happens depends *on whether the ductus opens above or below the constriction of the* aorta. If the opening is above the coarctation the shunt will be, as usual, from aorta to pulmonary artery. If below, then the pulmonary pressure may be higher, and the shunt will be from "right to left." In these circumstances the lower part of the body will be cyanosed, so that there is a remarkable contrast between the hands and the feet. In the former, with the ductus above, the operation is easy; otherwise it may be very difficult *(13)*. In any case, the ductus should not be ligated if it is below the constriction. In the non-cyanotic cases the probability of severe pulmonary hypertension developing is strong *(14)* In these cases the murmur may be systolic only and the diagnosis may be very difficult *(15)* Uncomplicated pulmonary stenosis would be no reason for leaving the ductus If there were cyanosis however it should not be touched *True mitral stenosis may be found The murmur may be atypical*, but care must be taken to exclude the functional murmur caused by the increased flow through the mitral valve. If mitral stenosis is there, ligation should not be done, for the ductus may be a useful safety valve *(13)*

PULMONARY HYPERTENSION In some cases there is a high pressure in the pulmonary circulation, as in atrial and ventricular septal defects, hyperkinetic in origin. This may reach 100 mm Hg and more, so that later on the pressure in the pulmonary artery may exceed the aortic with the result that the shunt is reversed. The cause in these cases of this rise in pressure is obscure. It would appear to be initiated by contraction of the muscular coats of the pulmonary arterioles *(16)* This spasm can be relaxed by acetyl choline *(17)*, and in any case the pressure may vary considerably in one person from moment to moment

It would appear that later on there is hypertrophy of the muscular

hypertrophy of the right ventricle and right axis deviation is seen in the cardiogram (*18, 20*).

REVERSAL OF THE SHUNT. When the shunt is reversed there is cyanosis, "differential cyanosis." The face and arms are less affected than the feet This may be present at birth (*19*), or appear later (*18*) The arteriolar resistance is raised. The *murmur* may be deceptive In some cases there is no characteristic Gibson murmur (*20, 21*). Only a systolic murmur may be audible, due to the flow from pulmonary artery to aorta (*22*), or the pulmonary valves may be incompetent, and only a loud diastolic murmur, even with a thrill, be noted (*17*) If the pressure be raised in the pulmonary artery the flow from the aorta will only be in systole, and so no diastolic component will be heard The pulmonary hypertension may appear as a gradual rise *pari passu* with the increased flow, but in some cases it seems to be present from the start (*23*) On the other hand, some observers do not consider that the increase in flow

point is that when the shunt is reversed it is better not to ligate the ductus (*20, 21, 24*) But if ligation is done earlier there may be a considerable fall in the pulmonary pressure

Course and prognosis. Although some patients may survive past the age of fifty, it is rare to meet them above the age of forty Two have been recorded over seventy and one over eighty (*33*) There was no thickening of the arterioles in the lungs (*25*). In about half the patients heart failure comes on and in a quarter

on starts at

the stream

From here

spread down to the valves In a very few instances the ductus may close spontaneously in middle life (*23*)

Differential diagnosis. In most cases the diagnosis is easy. It will be more difficult if the shunt is reversed, for the murmurs are atypical

from the aorta (*28*)

The Gibson murmur may be simulated by those due to other lesions as already noted such as

or an

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or a

complicated ventricular septal defect or even by large internal mammary arteries Venous hums may mimic the murmur *(29)*. A continuous murmur was heard in a complex case with stenosis of the right pulmonary artery and also ventricular and auricular septal defects *(32)*. The presence of arterial blood on the right side of the heart will be revealed in these cases. The site of the shunt may be indicated by the chamber in which it is first detected. But if the pulmonary valves are incompetent the diagnosis may be very difficult.

Ligation of the ductus arteriosus. The general consensus of opinion is that the ductus should be ligated in childhood. The result may be that the raised pressure in the pulmonary artery, if present, may fall. But if the pulmonary hypertension is associated with irreversible thickening of the pulmonary arterioles, ligation can do no good. This is likely to be the situation when there is established reversal of the shunt. The arteriolar resistance is raised but not the "wedge" pressure The vascularity of the lungs is decreased, the cardiogram shows severe right side predominance In border-line cases with nearly balanced pressures in the pulmonary artery and the aorta, the ductus may be clamped at operation, and the effect on the pressure in the pulmonary artery observed. If it rises ligation *should not be done (34). After ligation enlargement of the heart* disappears and the beat becomes quieter. The enlarged pulmonary artery will slowly decrease in size. The typical Gibson murmur will disappear, but for a time a systolic murmur from the dilated pulmonary artery will remain While some children seem to be but little affected by the patent ductus, others are weedy, ill-grown and somewhat backward. In these one can always count on improvement which is often dramatic. The risk of the operation is minimal, under 1% as a rule, nowadays. Recanalisation has been reported, but is rarely noted nowadays It will be impossible if the ductus is divided between ligatures, but this is technically a more difficult procedure. *If the ductus is infected operation should be carried* out as soon as possible after a course of penicillin, which need only be short The presence of cardiac enlargement indicates operation without delay, the apical diastolic murmur probably shows a large flow through the ductus which should certainly be tied *(26)* The [illegible] has been found to be high, for the mitral [illegible] relatively stenosed.

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2. Rossi, E *Herzkrankheiten im Säuglingsalter*, Stuttgart, 1954 p 182

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4 Record, R. G , McKeown, T. 1953. *Brit. Heart J.* 15, 376.
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6. Donzelot, E. et al 1950 *Acta Cardiol.* 5, 225.
7. Wood, P. 1950 *Brit. med. J.* 2, 639.
8 Lewes, D. 1952 *Brit Heart J.* 14, 357
9 Gross, R E , Longino, L A. 1951. *Circulation*, 3, 125.
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11 Taylor, B E *et al* 1950. *J. clin. Invest* 29, 745.
12 Voci, J *et al* 1951 *Arch Mal Cœur*, 44, 1103
13 [illegible]

18 Damman, J. F. *et al.* 1953 *Bull Johns Hopkins Hosp.* 92, 128
19. Smith, G 1954 *Brit Heart J.* 16, 233
20 Cosh, J. 1953. *Brit. Heart J* 15, 423.
21 Hultgren, H M *et al* 1953 *Circulation*, 8, 15.
22 Myers, G. S *et al* 1951. *Amer. Heart J* 41, 819
23. Campbell, M 1955 *Brit Heart J* 17, 511
24 Yu, P N *et al* 1954 *Amer Heart J* 48, 544
25 Fishman, L , Silverthorne, M L 1951. *Amer Heart J* 41, 762.
26 Pinto, T J 1955 *Amer Heart J.* 50, 1.
27 Vernant, P 1955 *Arch Mal Cœur*, 48, 277
28 Goetz, R H 1951 *Brit Heart J* 13, 242
[illegible] *Lancet* II, 272.
10, 363

[illegible] *et al* 1957 *Circulation*, 15, 865
33 Bain, C W C. 1957 *Brit Heart J.* 19, 574
34 d'Abreu, A L 1958 *Brit med J* 1, 957.
35 Neill, C , Mounsey, P 1958 *Brit Heart J.* 20, 61
36 Burhard, E D 1958 *Brit med J* 1, 806
37 Wilson, R R. 1958 *Brit. med. J* 1, 810.
38 Bonham-Carter, R E *et al* 1955. *Brit Heart J* 17, 255
39 Steinberg, I *et al* 1958 *Circulation*, 17, 372
40. Mark, H *et al* 1958. *Circulation*, 17, 359.
41 Heiner, C D., Nadas, A S 1958 *Circulation*, 17, 232

ABNORMALITIES OF THE CORONARY ARTERIES

The coronary arteries start to develop about the end of the second week of fœtal life, before the truncus arteriosus is divided by the spiral septum If, when the truncus is divided into the pulmonary artery and aorta, the buds forming the coronary arteries lie in front of the septum, they will be found to arise from the pulmonary artery.

Anomalies of the ostia are more common than those of distribution. The former are usually associated with other defects (7)

The left coronary artery is more often misplaced, and may arise from the pulmonary artery. The supply of venous blood causes degeneration and fibrosis and calcification in the myocardium (1). Considerable enlargement of the heart, with gallop rhythm, may result. The cardiogram may be abnormal, both in QRS and T waves A transmural infarct has been found in the front of the left ventricle in such a case at the age of three months (2). This lesion was shown by the cardiogram In another case of about the same age there were attacks of pain, sweating and breathlessness (3) The conclusion is that the supply of venous blood at low pressure causes the ischæmic lesions in the muscle (4). Patients with this defect do not live long.

While ill effects result from the origin of the left coronary artery from the pulmonary artery if the collateral circulation is not good, the results in other cases may not be so unfavourable The origin of the right coronary artery from the pulmonary artery is not incompatible with health and survival

A single coronary artery may arise from the aorta. This may be either the left or the right In one case, for example, the right supplied most of the heart, with a small branch round the front of the pulmonary artery to the left (5) This abnormality in itself does not matter If there are no other defects the person is no worse for it, and may reach old age Perhaps later on the development of coronary disease may have more serious consequences, as in the case of Dr Thomas Arnold, of Rugby, described by Latham many years ago, in his "Lectures on the Heart"

Absence of the left coronary artery seems to be associated with much ischæmic disease in the muscle, and infarction, if it does occur, is extensive (6).

Actually these abnormal coronary arteries are not particularly prone to develop sclerosis and lead to infarction later in life (7) Arterio-venous fistula may be associated with an anomalous coronary artery. It may show in an angiogram. Aortography is rather risky A continuous murmur is heard low down over the præcordium, rather variable in position. Cardiac pain may be felt (8)

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3. Fisher, H., Lloyd, O C. 1951. *Brit. Heart J* 13, 406.
4. Soloff, L. A 1942 *Amer. Heart J.* 24, 118.
5. Smith, J. C. 1950. *Circulation*, 1, 1169

6. Roberts, J. T., Loube, S. D. 1947. *Amer. Heart J.* 34, 188
7. Alexander, R. W., Griffith, G. C. 1956. *Circulation*, 14, 800.
8. Steinberg, I. et al. 1958. *Circulation*, 17, 372

✓DEXTROCARDIA

The heart lies on the right side of the chest, with the apex at the right. Strictly speaking, the word should not be used for cases in which the heart is displaced to the right because of pulmonary disease or elevation of the left half of the diaphragm. These types are better described as displacements.

The abnormality must arise very early in fœtal life. Cockayne considers that transposition is due to the formation of a sinistral instead of a dextral spiral in the viscera (1). Complete transposition of the viscera is inherited as a recessive character, and is determined by a single autosomal gene.

There are two varieties.

Dextrocardia with transposition of the viscera (*situs inversus totalis*). Here the heart is entirely reversed, the "mirror image" heart. In this case the arterial ventricle still forms the apex of the heart, but points to the right. This is the commoner variety. The electrocardiogram is characteristic. Lead I is completely inverted (mirror image), all the deflections pointing downward. Lead II and lead III are [illegible]

[illegible] dextrocardia. When other congenital defects are present this typical curve may be modified (2). The importance of the direction of P in lead I is great; it is the one quite reliable sign when it is clearly negative (5).

The skiagram is a mirror picture. The stomach lies to the right, and the liver to the left.*

Angina pectoris has been described in dextrocardia with radiation of the pain to the right arm. A similar distribution of the pain may occur [illegible]

[illegible] charac-

[illegible] those

[illegible] infarction

* "La nature ne [illegible]

[illegible] was the accour[illegible]

similar findings are seen. *Cyanotic heart disease is not uncommon in situs inversus totalis* (4).

Clinically, this form of dextrocardia, when there are no other lesions, causes no disability.

Isolated, uncomplicated dextrocardia, without transposition of the viscera. (a) The arrangement is the same as in total transposition of the viscera with inversion of the heart chambers; the arterial ventricle lying behind and to the right, and the venous in front and to the left. The cardiogram shows the usual "mirror image." The aorta may be right-sided. The abnormality is of no importance in itself if there are no other abnormalities But, in fact, in isolated dextrocardia they are usual, causing cyanosis; then the condition is said to be "complicated" (4).

(b) Heart chambers not inverted Here also, cyanotic lesions are common. The condition is rare. The venous ventricle, lying behind, forms the apex of the heart, and the arterial ventricle lies in front No "mirror image" is therefore present. The abnormality probably rises later in intrauterine life than the other.

Actually two types are possible. (a) The venous atrium is on the right as usual. The superior vena cava may be found on both sides. The P wave is positive in standard lead I (5, 6) The arterial ventricle *is mainly to the right and behind, and the venous to the* left. If the heart lies vertically, the arterial ventricle may be lower and the venous mainly above and to the right (6) (b) If the heart is actually transposed, the superior vena cava and venous atrium will be on the left and the P wave in lead I negative (5). Septal defects are common here.

An additional help in differentiating these cases is the cardiac catheter (7). This can be better carried out from the right arm

Lævocardia. Isolated inversion of the abdominal viscera may be associated with congenital cardiac defects, both atrial and ventricular (5) These are usually multiple and bizarre, so that diagnosis is difficult (8). The venous atrium and the superior vena cava may be transposed with the abdominal viscera. In standard lead I the P wave will then be negative. More rarely the venous atrium and venæ cavæ are on the proper side, and P is then positive

There may be transposition of the aorta and pulmonary artery, and abnormalities of the great veins as already mentioned Then there will be *pulmonary plethora. Otherwise there is a tendency to* inadequate flow of blood to the lungs, for which a Blalock operation might be indicated, but there may be serious technical difficulties, and mortality may well be high (8).

1 Cockayne, E. A. 1938. *Quart. J. Med.* 27, 479
2 Cain, J C 1945. *Amer Heart J.* 30, 202.
3 Soulié, P. *et al* 1952. *Sém Hôp. Paris* 28, 1.
4 Campbell, M , Reynolds, G 1952. *Brit. Heart J.* 14, 481.
5 Campbell, M , Forgacs, P 1953 *Brit Heart J.* 15, 401.
6 Gubbay, E. R. 1955. *Amer. Heart J.* 50, 356.
7 Chapman, C. B , Gibbons, T. B. 1950 *Amer. Heart J.* 39, 507.
8 Young, M D., Griswold, H. E. 1951. *Circulation*, 3, 202.

ARTERIO-VENOUS ANEURYSM OF THE LUNG

Tumours form in the lungs in which there is a mass of vessels with free communication between those derived from the pulmonary arteries and those from the pulmonary veins They vary a good deal in size, and may be as large as an orange. For the most part they are in the middle or lower lobes (*1*)

Clinical features. Cyanosis may not be present at first (*3*) but increases once it has appeared The arterial oxygen saturation may be as low as 60% (*4*) There are the usual associated abnormalities such as clubbing of the fingers and toes and polycythæmia Dyspnœa becomes severe Cough is frequent, and there may be hæmoptysis Seizures of cerebral origin are common, and so is fainting Sometimes there are no symptoms at all (*2*).

In some half of the cases murmurs, continuous, of the Gibson type or sometimes only systolic, are heard over the lungs (*4*). On forced expiration the murmur becomes softer and shorter. Inspiration increases it (*2*). The right ventricle of the heart may be enlarged, there are no actual cardiac murmurs (*3*).

The output of the heart may be increased: there is a rise in th

The cardiograms may show preponderance of the right ventricle. In most recorded cases there are cutaneous telangiectases as well

Vascular tumours of the thoracic wall may

ually there are.

Failing that relief, once symptoms come on, the danger lies in pulmonary infection, hæmoptysis and heart failure.

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4. Baer, S. *et al.* 1950. *Circulation*, 1, 602
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6. Maier, H. C., Stout, A. P. 1950. *Circulation*, 1, 809

Idiopathic dilatation of the pulmonary artery. This is a very rare congenital abnormality when it occurs alone. In simple valvular pulmonary stenosis; atrial septal defect; patent ductus and ventricular septal defect where the flow is increased, and the pressure may be raised, it is usual to find varying degrees of enlargement

In the idiopathic type the whole pulmonary tree may be dilated and the aorta hypoplastic. The whole of one branch and its own branches may be huge and pulsate freely on the screen, particularly if the pulmonary valves are incompetent (*1*). In these cases there is a loud systolic murmur and thrill in the pulmonary area. The closure of the pulmonary valves is loud and palpable The valves may be incompetent. The right ventricle will then be enlarged Sometimes there is no pulsation and the peripheral lung fields are normal. A clicking sound may be heard over the artery early in diastole (*2*) The skiagram will show the large artery The cardiogram will be normal and so will the pressures in the right ventricle, unless there is pulmonary incompetence (*3, 4*) The valves may be bicuspid. The artery being very thin may rupture Its diameter may be from 40–50 mm There are no symptoms, unless the pulmonary valves are incompetent. Pressure on the bronchi may lead to infection

1. Kaplan, B M. *et al.* 1953. *J. Lab clin Med* 41, 697
2. Leatham, A., Vogelpoel, L. 1954 *Brit Heart J.* 6, 21
3. Goetz, R. H , Nellen, M. 1953 *S Afr. med J.* 27, 360.
4 van Buchem, F. S. P. *et al* 1955 *Dis. Chest* 28, 326

Aortic origin of right pulmonary artery. The normal pulmonary artery on this side may be wanting. The anomalous vessel arises from the aortic arch. This does not affect the function of that lung. The defect may be found by angiocardiography There are no particular physical signs. A patent ductus is frequently an associated lesion (*1*) Cyanosis may be present if associated right to left shunts are present (*2*)

1. Caro, C. *et al.* 1957. *Brit. Heart J.* 19, 345.
2. Maier, H. C. 1954. *J. thorac. Surg* 28, 145.

STENOSIS OF THE PULMONARY ARTERY

This may appear alone, or with other defects such as valvular pulmonary stenosis (*1*) The defect has been likened to coarctation of the pulmonary artery (2) Sometimes a branch only is stenosed, or there may be multiple constricted areas. A systolic murmur and thrill are the signs, but cannot be distinguished from other lesions causing such signs without the help of the cardiac catheter and angiocardiogram It might be important to diagnose this lesion if it were present with pulmonary stenosis as well, for it might escape the surgeon's attention. The cardiac catheter will show the presence of a sudden rise in pressure as it is pulled from the periphery of the lung Akin to this is unilateral obscure hypoplasia of the main branch which may be absent entirely.

Absence of main branch On one side, usually the left, but occasionally the right, the main branch may be missing altogether (3). The chest is rather smaller on the affected side, for the lung is smaller The skiagram may show a lesser translucency or may appear deficient in vessels (*4*) The blood supply comes from bronchial arteries and anomalous vessels This lung, of course, plays practically no part in the oxygen exchange Although handling 37% of the inspired air it may only be responsible for 6% of the uptake of oxygen (3) The pressures in the pulmonary artery are normal at rest, but rise excessively on exercise The right ventricle is not enlarged even at sixty years Patients are liable to cough and hæmoptysis (*4*) While the abnormality in itself is not serious it may be important if extensive operation on the sound side is contemplated Other defects are found as well, such as the Tetralogy of Fallot and right-sided aortic arch (*6*)

1 Williams, C B et al 1957 *Circulation*, 16, 195
2 Coles, J E Walker, W J 1956 *Amer Heart J* 52, 469
3 Madoff I M et al 1952 *New Eng J Med* 247, 149
4 Elder J C et al 1958 *Circulation*, 17, 557
5 Smart, J , Pattinson, J N 1956 *Brit med J*, *i*, 491
6 McKim, J S , Wigglesworth, F W 1954 *Amer Heart J* 47, 845.

CONGENITAL HEART BLOCK

About the fifth week of fœtal life the anterior and posterior endocardial cushions fuse to form the atrio-ventricular canal As the atrial ring develops the *muscle* of the auricle and ventricle is

separated except for the fibres which become the bundle of His. The bundle may be interrupted by fibrous tissue in this process Actually, the septum is completed at the eighth week, and the hole, if present, will be anterior to the membranous part; hence most cases of patent septum are seen without heart block. But it has been noted that when the membranous part is affected there may be heart block, for the bundle lies near. Probably the important point is involvement of the upper part of the bundle or node in excessive fibrosis. Atrial septal defect may be present as well.

Clinically, these cases may easily escape diagnosis for the ventricular rate is often over 80. The lesion has been diagnosed in utero by means of sound records. The blood pressure may be rather high. There may be a fair degree of acceleration on exercise. Atropine may cause a considerable increase in rate. Adrenalin may not accelerate the heart, but the rate may rise with fever. In this case there was congenital dextrocardia *Stokes-Adams attacks* are rare, but syncopal attacks in childhood should arouse suspicions of the condition. The patients are not likely to die suddenly, and they have very fair capacity for exertion (*1*). Isolated congenital heart block is no bar to pregnancy.

The prognosis appears to be very good if no other lesions are present. *Other lesions are added abnormalities, and do not cause the block*; they are really parallel disturbances (*1*) The association with ventricular septal defect is to some degree true, but not so close as has been stated in the past

1. Campbell, M, Thorne, M G 1956. *Brit Heart J* 18, 90.

ENDOCARDIAL FIBROELASTOSIS

As these cases appear very early in infancy, and have been noted among the newborn, it is right to class them as congenital, though some are found later on in life (see p 162) The incidence is equal in girls and boys (*1*)

Morbid anatomy. There is a remarkable white thickening of the endocardium This is due to overgrowth of fibrous tissue and elastic tissue, collagen fibres are profuse There is no true inflammatory reaction. The fibrous bands may spread among the muscle fibres adjacent and these may appear atrophic The distribution of the fibroelastosis varies a good deal. *The thickness may be several millimetres*. There may be a little calcification The inner wall of the left ventricle is mainly affected in almost all cases (*3*), but the right

y be affected as well. In many cases, perhaps 30–50% (2), the lves are abnormal too. The mitral and tricuspid are more comnly attacked than the aortic; but these may not escape. The lves become thick and show myxomatous degeneration (2). The ordæ tendineæ and papillary muscles may be thick and fused (1), that the valve may be severely stenosed There is some doubt as the nature of the valvular lesion, for here no elastic tissue appears. his thick fibrous sheet seems to interfere with the filling and nptying of the ventricles, particularly checking diastole (4). ccasionally the auricle is affected too Mural thrombosis may occur nd give rise to embolism (5)

an be excluded, nor does it appear to be a collagen disease for the nyocardium itself is little involved (6). Actually it has been pointed out that the process of fibroelastosis closes the ductus arteriosus and the mammary and uterine arteries The most feasible suggestion is that anoxia may be the cause (2, 7). There

it were a general disease (8) But no explanation is adequate so far.

The diffuse endo-myocardial fibrosis of adults, and the somewhat similar disease seen in Africans has a different histology (see p. 162), the disease of infants is a definite type (9) Other cases suggest that the infantile type may survive to adolescence (10)

Clinical features. The symptoms are indefinite They depend on the age There may be fatigue, dyspnœa and tachycardia (11) The enlargement becomes very obvious and the outline of the heart is globular Murmurs vary a good deal Probably they are present in about 20–30% of cases (3, 11) The cardiograms vary, sometimes they are normal (11) or there may be curves of the bundle branch

been found Possibly cortisone might be useful Digitalis has little power against the failure .

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2 Kempton, J. J, Glynn, L. E. 1955. *Quart J Med* 24, 109
3 Dennis, J L *et al.* 1953 *Pediatrics*, 12, 130.
4 Lewis, K C 1951 *J. Pediatrics*, 39, 698.

5 Thomas, W. A. *et al.* 1954. *New Eng. J. Med.* 251, 327.
6. Adams, F. H., Katz, B. 1953. *J. Pediatrics*, 41, 141.
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8. Gibbs, N M. *et al.* 1957. *Brit Heart J.* 19, 193.
9. Lynch, J B., Watt, J. 1957. *Brit. Heart J.* 19, 173
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11. Blumberg, R. W., Lyon, R. A. 1952. *Amer. J. Dis Child.* 84, 291.

ANOMALOUS THORACIC VEINS. PULMONARY AND CAVAL

The veins draining the lungs may present several anomalies of development; and these vary a good deal in their clinical importance. The venæ cavæ also may be abnormal

Embryology. GREAT VEINS. In the ordinary course of growth the part of the left precardinal vein caudal to the innominate vein disappears, remaining only as the ligament of Marshall The coronary sinus and the oblique vein of Marshall represent the left part of the sinus venosus If the left precardinal vein persists, it will appear as a left superior vena cava draining the innominate, jugular and subclavian veins on the left side, and entering the right atrium at the coronary sinus through the duct of Cuvier. If the right superior vena cava is missing the right innominate vein will join those on the left. A sole persistent left superior vena cava may persist without one on the right side (*1*). The *pulmonary veins* may fail to develop normally so that all or some of them may run into the right atrium or superior vena cava Normally the common pulmonary vein disappears, and the four branches enter the left atrium, if the pulmonary fold is formed defectively, their relationship to the developing septum becomes anomalous (*13*).

To sum up, the pulmonary veins may all run directly into the right atrium, or only those from the right lung. They may drain into the coronary sinus, or into a left superior vena cava which crosses to *join* the *innominate* vein, right superior vena cava and so into the right atrium.

It is important to remember that if all the pulmonary veins drain into the right atrium, the atrial septum must remain patent and the shunt will be from right to left The size of this defect will be important The left atrium will be small (*2*) The complete transposition of pulmonary veins to the right side is more serious than the partial (*3*) The transposition of one vein is not important (*13*). The right pulmonary veins are more usually affected when there is partial transposition.

PARTIAL TRANSPOSITION OF VEINS. It is not uncommon to find that one or both of the veins from the right lung drain into the right atrium Perhaps one-half of the cases are associated with an atrial septal defect (*13*) The vein is likely to be found on cardiac catheterisation when the catheter may enter the vein (*14*). The blood in the right atrium will be highly oxygenated in contrast to that in the venæ cavæ If the right pulmonary veins enter the superior vena cava the highly oxygenated blood will be found there. The atrial septal defect is high, and there is likely to be a small shunt through it into the left atrium from the superior vena cava, but not from the inferior (*19*) The vein may be revealed in the angiocardiogram (*9*) No symptoms are likely to arise from a single anomalous vein (*12*, *14*), and the outlook is good If the abnormal drainage affects at least one lung there may be adverse effects (*13*) The output of the right ventricle is increased and the right side enlarged In some instances pulmonary hypertension has developed. In almost all respects the cases resemble those with atrial septal defect, for the effects of the lesion are, in fact, in *causing* a left to right shunt as arterial blood enters the right side If there is an atrial septal defect as well the results will be worse A single anomalous vein need not be treated surgically, unless a defect in the atrial septum is also being closed at the same time.

COMPLETE TRANSPOSITION These patients are stunted and weakly, and easily become breathless. They are liable to pulmonary infection, and are apt to be cyanosed The right atrium and ventricle are enlarged There must be a defect in the atrial septum, and this is usually posterior (*13*) Most of the blood will flow up the *pulmonary* artery, which pulsates freely, and there is pulmonary plethora (*5*) There is usually a systolic murmur over the pulmonary artery (*8*, *11*); the sound of the closure of the pulmonary valve is loud and the second sounds at the base are *double* (*1*) The *cardiogram* shows hypertrophy of the right ventricle, with curves indicating delayed activation of its surface (right bundle branch block) (*6*, *7*, *11*) There may be atrial fibrillation. In fact the features are very much [illegible]

[illegible] the blood [illegible] n fact the [illegible] saturation of the *blood* in the right ventricle, pulmonary artery and systemic arteries may be the same (*12*) (Fig 26)

The angiocardiogram may show a jet of blood interfering with the opacity of the shadow of the right auricle (*11*)

In the course of time there may be pulmonary hypertension

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ANOMALOUS THORACIC VEINS. PULMONARY AND CAVAL

The veins draining the lungs may present several anomalies of development; and these vary a good deal in their clinical importance *The venæ cavæ also may be abnormal.*

Embryology. GREAT VEINS. In the ordinary course of growth the part of the left precardinal vein caudal to the innominate vein disappears, remaining only as the ligament of Marshall The coronary sinus and the *oblique vein of Marshall represent the left part of the* sinus venosus If the left precardinal vein persists, it will appear as a left superior vena cava draining the innominate, jugular and subclavian veins on the left side, and entering the right atrium at the coronary sinus through the duct of Cuvier If the right superior vena cava is missing the right innominate vein will join those on the left. A sole persistent left superior vena cava may persist without one on the right side *(1)* The *pulmonary veins* may fail to develop normally so that all or some of them may run into the right atrium or superior vena cava. Normally the common pulmonary vein disappears, and the four branches enter the left atrium, if the pulmonary fold is formed defectively, their relationship to the developing septum becomes anomalous *(13).*

To sum up, the pulmonary veins may *all* run *directly* into the right atrium, or only those from the right lung They may drain into the coronary sinus, or into a left superior vena cava which crosses to join the innominate vein, right superior vena cava and so into the *right atrium*

It is important to remember that if all the pulmonary veins drain into the right atrium, the atrial septum must remain patent and the shunt will be from *right to left* The size of this defect will be *important*. The left atrium will be small *(2)* The complete transposition of pulmonary veins to the right side is more serious than the partial *(3)* The transposition of one vein is not important *(13)* The right pulmonary veins are more usually affected when there is partial transposition.

Persistent left superior vena cava and anomalous pulmonary veins. All the pulmonary veins may drain into a left superior vena cava The veins from the right lung cross behind the heart to join those from the left to form a large arching vein which passes up and across in front of the aorta and pulmonary artery over to the right side to join a single right superior vena cava there The heart lies free and can be lifted up from its bed. The presence of this

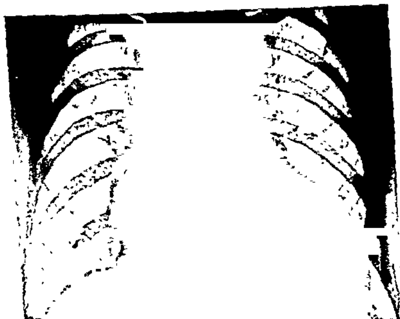


FIG 27 Persistent left superior vena cava draining pulmonary veins Note cap formed by dilated S V C surrounding aortic knuckle

huge venous arch give the characteristics peculiar to the condition The venous drainage in its effects is similar to that already described for the right auricle, except that the cardiac catheter shows the pressure of highly oxygenated blood in the superior vena cava, and of course in the right auricle, but normal in the inferior vena cava The X-ray appearances are typical The heart shadow is more or less enlarged and there is pulmonary plethora The oval shadow of the abnormal vena cava is seen above that of the heart Its density is less and the aorta and pulmonary artery show through it, and there

Cyanosis, of central type, increases. Fatal heart failure comes on rapidly (*13*), in middle life or earlier.

Persistent left superior vena cava. If there is no other abnormality this usually opens through the duct of Curvier into the coronary sinus. The right superior vena cava drains into the right



FIG 26. Catheter in anomalous pulmonary vein draining into right atrium.

atrium as usual. This abnormality is of no importance It may be in the way during operations on the heart.

The catheter passes easily into the right atrium, through the duct of Cuvier, but it cannot be made to take the acute angle required to enter the right ventricle The right arm may prove more easy, but here there may be difficulty in getting it to take the bend into the right superior vena cava Sometimes it may be necessary to use the femoral vein (*10*)

CHAPTER 2

INFECTIONS OF THE HEART, AORTA AND PERICARDIAL SAC

In this chapter it is convenient to consider together various subjects which are usually discussed separately. Their ætiology is mainly concerned with infection, and anatomically the heart valves are usually affected. Pericarditis is considered here because some aspects of rheumatic pericarditis are similar to those of other origin. Infections which mainly damage the myocardium are dealt with in the next chapter.

RHEUMATIC CARDITIS

Rheumatic carditis is the most important manifestation of rheumatic fever. Chronic carditis is the only serious sequel of the disease, as its other manifestations are self-limiting and reversible.

It is difficult to define cause when host reactivity plays an important part in the disease process, but all recent work has confirmed that infection with the group A hæmolytic streptococcus is the precipitating factor (*1*). It is probable that the disease process is independent of the survival of streptococci, however, it has been established that even when antibiotic therapy is delayed for nine days after the acute infection, the incidence of *rheumatic fever* is sharply reduced (2). The consensus of opinion is, in any case, that some sort of antigen-antibody reaction is involved, and that the streptococcus, or some part of it, is the antigen.

The ultimate extent and degree of cardiac damage is in large measure positively related to the duration, severity and number of recurrences or exacerbation of attacks. There is no evidence of immunity to the rheumatic reaction provoked by streptococcal infection, if anything there is an increased susceptibility to the reaction once it has been experienced. It is clear that prevention of recurrent streptococcal infection is important in prevention of ultimate valve scarring and it has been clearly shown, largely in the United States, that this may be achieved by the *prophylactic use of penicillin* (or sulphonamide). The mean recurrence rate of rheumatic attacks was almost five times as great in an unprotected

is a narrowness between it and the shadow of the heart below as a rule (*1, 3, 5, 15*) This double shadow has been likened to a "figure of eight," a "dumb bell" and a "cottage loaf," so it must be said to vary somewhat (Fig. 27). Angiocardiography is of little value, as the material becomes so rapidly dilated. The possibility of surgical correction of this abnormality is very small The left auricle is usually underdeveloped, and the vein is very large with thin walls.

Other variations also occur. Not all the pulmonary veins may enter this persistent superior vena cava In this case the appearances are less striking (*1*) The pulmonary veins may enter the right superior vena cava, or the inferior vena cava, or even the portal vein. In these circumstances there is a right to left shunt through the atrial septum: the pulmonary artery is large and so is the liver. The left auricle and ventricle are small (*16*). In another case the heart was trilocular and there were other defects, such as a patent ductus (*17*)

Sometimes the coronary sinus may receive the pulmonary veins (*11*) The left superior vena cava may drain into the left auricle. There will then be a large defect in the atrial septum In spite of this the abnormality does not seem to be important It may be more convenient to use the right arm for the cardiac catheter in these circumstances.

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(6, 7). The mitral diastolic murmur is often soft and follows the physiological third heart sound; it is low pitched and often short (Fig 28)

Aortic valvulitis is recognised by finding an early diastolic murmur at the left sternal edge. The systolic murmur of aortic valvulitis cannot be distinguished with certainty in the vast majority of cases from an innocent ejection murmur (Fig. 28). Severe aortic incompetence or mitral incompetence may develop in a first attack

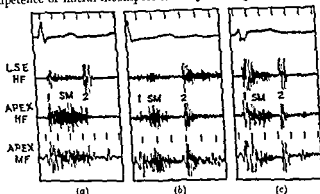


Fig. 28. Phonocard—

but rarely produces much enlargement *before six to eight weeks* of continuous activity, so that cardiac enlargement must be considered a relatively late sign.

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10 … had some bradycardia, unrelated to salicylates, at some period of the first five weeks in hospital and 11% of these developed persistent valvulitis (8)

Pericarditis shown by pain, friction or effusion is certain evidence of carditis, but this *only* occurs in some 10–15% of all cases. The finding of dry pericarditis indicates carditis but it is a relatively unimportant feature compared with the development of effusion (9) which may appear at any time from the first week onwards. A raised venous pressure and signs at the lung bases pointing to the development of effusion may precede X-ray evidence. The lung

control group as in protected ones over a five-year period (3) A report of the Rheumatic Fever Committee of the Royal College of Physicians (4) recommends that *any child with rheumatic fever should be given penicillin for five years, or until leaving school, whichever is the longer*, any patient who has had rheumatic fever should receive penicillin when there is special risk, i e. on entering hospital or any semi-closed community such as an army camp, etc Oral penicillin (crystalline G) 200,000 units twice daily, or (penicillin V) 120 mg. twice daily is effective, but even when carried out conscientiously infection is still possible. A single injection of benzathine penicillin G (1,200,000 units) per month is also recommended as adequate protection Over 2000 airmen exposed to streptococcal infection were given 100,000 units of benzathine penicillin; this procedure resulted in a prompt significant decrease in streptococcal disease and protection lasted for twenty-five days (5) A definite streptococcal infection in any patient at risk to further rheumatic fever should be treated as a matter of urgency with bactericidal antibiotic therapy.

Clinical Features of Rheumatic Carditis

These are well known, but work during the last decade has shown that less reliance should be placed on some signs, whilst others deserve more emphasis especially in an early diagnosis of first attacks. *Apart from the history and evidence of arthropathy*, erythema marginatum and nodules are confirmatory evidence of the presence of the rheumatic state Nodules do not appear before the fifth week of activity.

The best evidence of early carditis is provided by auscultation (6, 7). In the majority of cases the diagnosis of carditis is made by finding significant murmurs which indicate valvulitis; the only exceptions are those few patients whose sole evidence of heart involvement is pericarditis or a prolongation of the P-R interval (7%). Murmurs of valvulitis may appear within 24 hours of the onset of the disease; they are often very soft and localised, sometimes disappearing during the course of the attack, but their presence always indicates that the heart is affected.

Mitral valvulitis is recognised by finding either a systolic or diastolic murmur or both The systolic murmur is rather high [illegible] and continues through systole to

[illegible]

from the [illegible] sternal edge or over the pulmonary artery in almost every child

The P-R interval is prolonged in 30% before the start of treatment (17), and in a smaller proportion the clinical counterpart of this change—a softening of the first heart sound is detectable. Rarely complete A-V dissociation is seen (15) and there is a recent report of heart block leading to Stokes-Adams attacks in active carditis (19) (Fig. 30)

Treatment. Advances in the treatment of rheumatic fever have not equalled the advance in its prevention by antibiotic prophylaxis

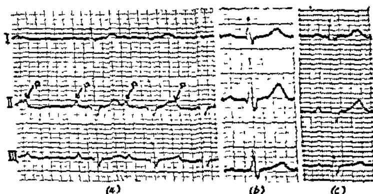


FIG 30 Rheumatic carditis Electrocardiograms showing (a) Heart-block with Wenckebach phenomenon, (b) Same patient showing slight prolongation of PR interval *one month later* and (c) Normal conduction *one year later*

and social betterment Rest in bed remains the most widely agreed and helpful measure for patients with active carditis, it should continue for two weeks after clinical signs of activity have subsided and the sedimentation rate has been normal, followed by a slow graduated return to full physical activity Education facilities should be provided for children where long stay in hospital is indicated

The joint United Kingdom-United States scheme for studying the effects of cortisone, ACTH, and aspirin showed no ... d...

... found that signs and symptoms were arrested rapidly with 320–400 mg. of oral cortisone a day

signs are due to pleural effusion. Tachypnœa is usual Temperature, pulse rate and sedimentation rate usually rise. Abnormal electrocardiograms were present in only 10 of 17 cases of rheumatic effusion. The prognosis in cases with effusion is worse in children under ten years, and when there is long continued activity; after recovery there are usually signs of residual valvulitis (Fig. 29).

Heart failure is not an early sign of carditis; it is rarely seen in first attacks and then only in severe cases after weeks or more of

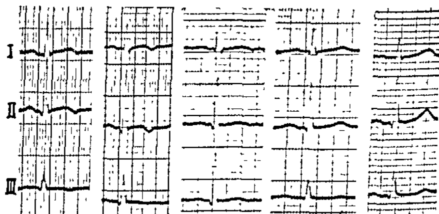


FIG. 29. Rheumatic pericarditis Electrocardiogram standard leads only taken at monthly intervals and showing gradual correction of S-T deviation and T-wave inversion.

continued activity Differential diagnosis from effusion may be difficult; apart from the clinical features, a low sedimentation rate in failure is a useful contrast to a raised figure found in effusion. Digitalis therapy may give an excellent response but in general the prognosis is grave, especially when response to treatment is poor.

The electrocardiogram in rheumatic carditis. Earlier work on the duration of electrical systole (Q-T interval) suggested that its prolongation was the best criterion of rheumatic activity (*10, 11, 12*) and further, it was considered to reflect the extent of damage and thus aid prognosis (*13*). In one series the Q-T interval was prolonged above 0·405 in 100% and above 0·422 in 84% in active carditis, whereas control figures were 44% and 8% (*14*) Other work has suggested that positive correlation with activity is not very close and the frequency of prolongation is not very high (*15*) It is probable that QTc prolongation parallels activity in a significant proportion of cases, perhaps two-thirds to three-quarters, but insignificant changes occur in many cases with severe carditis (*16*)

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DISEASE OF THE MITRAL VALVE

Acquired mitral valve disease. This is mainly the result of rheumatic fever. It is occasionally due to other collagen diseases, especially lupus erythematosus (see p. 160). Endomyocardial fibrosis may also involve the papillary muscles, chordæ and even cusps, and result in organic mitral incompetence (see p. 162). Elaborate clinical, pathological and hæmodynamic investigations associated with studies of mitral valve surgery and its results, have led to more accurate diagnosis of the anatomical abnormality and resulting physiological disorder.

Anatomical and physiological features. The essence of mitral stenosis is the narrowing of the valve orifice, and it is clear that the severity of the patient's malady is, in the final analysis, mainly due to the severity of the obstruction. Although much has been known of the anatomy of the normal and abnormal mitral valve, recent detailed studies have shown that the whole valve mechanism is complicated, and that its various parts may be affected separately, or as a whole (*1*, *2*). There is evidence to show that progressive post rheumatic sclerosis is not due to inflammation and cicatrisation within the cusps, but rather to organisation of repeated fibrin deposits on the cusp surface between the commissures and on the chordæ (*3*).

The mitral valve has two cusps, the antero-medial one being large; both are attached to the fibrous atrio-ventricular ring. Two papillary muscles lie opposite the commissures and pass into the chordæ tendinæ which split to gain attachment to each opposing leaflet. Fine chordæ are inserted into the free margin of the valve and thicker ones fuse with the ventricular surface of each cusp. The fundamental narrowing which produces significant stenosis occurs at the cusp margins in the two opposing critical areas of tendon insertion (*1*). The rheumatic process may be largely confined to the valve margins, so that although the central pathway is greatly reduced to say 1 cm. × 0.5 cm., the valve cusps may remain supple and the chordæ almost normal. In more severe rheumatic

for seven days, or 240–320 mg of oral hydrocortisone for the same period In the period 1930–1955 it was found that the average duration of carditis was less than one month in only 20%, two to four months in 30%, more than four months in 50% and residual cardiac damage was present in all. In patients receiving the high dosage hormone régime for seven days, the duration of *active carditis was less than one month in 69%. There was no overt* evidence of residual damage following first attacks in 84% of these treated patients. When cortisone, salicylate and a combination thereof are compared it is clear that the hormone, or a combination, causes a more rapid fall of sedimentation rate (*25, 26*) After comparing six forms of treatment in 200 cases, Illingworth's group conclude firmly that cortisone cases fare better than all other cases with respect to carditis (*25*) However, high dosage hormone therapy or high dosage salicylate in combination with hormone are treatments not without considerable danger Although Bywaters states (*27*), after reviewing the position, that "It is still far from clear whether salicylate, steroid, a combination thereof, or bed rest alone offers the best chance of escaping residual valve deformity and even less clear what is the best dosage level to employ," most other authorities agree that hormone therapy is superior to salicylate, and that a combination is superior to cortisone alone, at least *in the active and early stages of the disease*

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of the pulmonary artery and the right ventricle. Although these two facets of obstruction at the valve are closely related, they are not totally dependent on each other and must be considered separately in every case



FIG. 31 Pure mitral incompetence, thickened mitral valve ring admitting three fingers. View from left atrium.

"wedged pulmonary arterial" or indirect "left atrial pressures" are recorded properly they correlate closely with recordings of direct left atrial pressures made simultaneously at operation, or by a percutaneous or trans-bronchial route (*10, 11, 12, 13, 14*)

The indirect left atrial pulse tracing shows "a" and "v" waves giant "a" waves are not common and the "v" ...
than "a" L...
(5) Mean le...
mitral steno...
moderate tc...
occurs when ... reach 30 mm Hg or more, but much higher pressures may be tolerated for a short time, i e during effort tests (4) The height of the left atrial pressure is directly related to the

infection, fibrosis affecting the whole cusps, the chordæ, and even papillary muscle occurs; sometimes there is cross fusion between sets of chordæ on each side of the cusp. The whole may become a thick fibrous mass in which the pathway is not only greatly narrowed and elongated, but no longer capable of any valvular function The main site of damage in valvulitis may be used for an anatomical classification (2) In the *commissural type* the leaflets and chordæ are usually affected, calcification may occur, but one commissure only may be mainly involved In the *cuspal type* the leaflets are mainly affected and grossly thickened, whilst in the *chordal type* gross fusion and shortening occurs so that a funnel is produced Various degrees of combination occur; in the most severe cases there is fusion of all parts. Calcification is more common in the valve leaflets than in the commissural junctions (2).

In pure stenosis the size of the orifice at operation is usually 1 cm × 0 5 cm (*1*, *4*). The range of size between which symptoms are first produced and that which is incompatible with life is from a valve length of 1·75 cm to some 0 5 cm, but such a small range is obviously associated with a much greater range in orifice area. When there is mitral incompetence the critical size is larger and in patients selected for operation the range was from 1·25 to 2 cm. by 0 75 to 1 cm (*4*) Significant regurgitation does not occur with a mitral valve area of less than 0·8 sq. cm. (*5*) (Fig. 31).

In organic mitral incompetence the valve is often more severely damaged than in stenosis, and may be no more than a rigid hole in a rigid diaphragm. The orifice may be 2·5 cm. or more long, by 1 cm Gross calcification is sometimes present and the whole valve unit from atrial endocardium to papillary muscles may be a thick rigid fibrous mass with extreme shortening of the chordæ. In such cases the evidence for a rheumatic ætiology is rather slender (*6*).

Hæmodynamics. Cardiac output is reduced in the majority of patients with mitral stenosis which is severe enough to produce symptoms (*4*, *5*, *7*, *8*, *9*) This is due to obstruction at the valve and in the lung In the large series reported by Wood (*4*) cardiac output averaged 3·8 litres/min in the surgical cases it was higher in those with normal rhythm (4·1 litres/min.) than in those with atrial fibrillation (3·6) and higher in those with paroxysmal dyspnœa and pulmonary œdema (4·0 and 4·6), it was very low (3 3) in patients with mitral facies

Obstruction of the mitral valve results in a rise of pressure in the left atrium and pulmonary veins, whilst obstruction in the lesser pulmonary arteries and arterioles results in a rise in pressure

lungs The vessels are constricted and undistensible, and are the seat of intimal proliferation. Foci of medial hypoplasia or aplasia are common, and these deficiencies are thought to provoke proliferation in the presence of hypertension In spite of these structural changes there is much evidence of a reversible functional mechanism as well. Certain ganglion blocking drugs, acetylcholine (*21, 22, 23, 24*) and successful valvotomy (*1, 25*) result in a fall of pulmonary vascular resistance, even in patients with an extremely high resistance. A fall in resistance from acetylcholine leads to a rise in left atrial pressure without significant changes in cardiac output, blood pressure or pulse rate Pulmonary vascular resistance probably increases with effort in some patients, and when the resistance is high, effort may cause a disproportionately great rise in pulmonary artery pressure. High pulmonary vascular resistance is positively correlated with severe pulmonary hypertension, low cardiac output, a relatively low arterial oxygen saturation and congestive heart failure. A high pulmonary vascular resistance is only found in patients with severe stenosis

In pure mitral incompetence it is uncommon for the pulmonary artery pressure or the pulmonary vascular resistance to be raised Ho—

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rap... collapse to near normal diastolic levels Left atrial and left ventricular pressure curves taken at mitral valvotomy and compared with the amount of incompetence found by the surgeon, showed that the height of the "v" wave, the v-c difference, and the Ry/v ratio were not helpful in recognising incompetence, a so-called "correlated x descent" of over 5 mm Hg indicated mitral incompetence (*16*) Dye dilution curves provide valuable evidence concerning the presence and degree of incompetence (*26, 27, 28*) The appearance time of dye is shortened and the spread of dye particles is increased for any given cardiac output and volume. Korner and Shillingford do not claim that small amounts of regurgitation may be detected, but the method can separate those who clinically and surgically had little or no regurgitation from those

...ynamic data available ... , and if necessary, hæmo.

degree of stenosis when the pulmonary resistance is not in the extreme range. When there is mitral stenosis combined with incompetence, the systolic wave tends to be *higher and to rise and fall more abruptly* than in pure mitral stenosis. Owen and Wood *(63)* found the most stable expression of the rate of the descent of the "v" wave, and thus an expression of the degree of obstruction, was the quotient of the calculated rate of fall divided by the height of the preceding "v" wave (Ry/v ratio) A value greater than 1·6 is unlikely to occur if stenosis is pure, or associated with only trivial incompetence There are limitations in measuring the "v" wave when pressures are normal or low, and the Ry/v is essentially an expression derived from an abnormal situation when the diastolic part of the left atrial curve is raised. There is some evidence that correlation of Ry/v with degree of obstruction and incompetence found at operation is not very close *(5, 15, 16)*

Pulmonary artery pressure The majority of patients with mitral stenosis severe enough to produce symptoms have a raised pulmonary arterial pressure. A slight increase in pulmonary capillary pressure is associated with a comparable rise in pulmonary arterial pressure, but a disproportionate rise occurs when the capillary pressure reaches 20–25 mm. Hg *(7)* The systolic pulmonary arterial pressure is above 100 mm Hg in a few patients, but the average was 60/63 mm Hg in 150 patients selected for operation *(4)*. The *pulmonary artery pressure always rises on effort, it parallels the* pulmonary capillary pressure in patients with a normal vascular resistance. High pulmonary artery pressures may fall with certain drugs (*vide infra*) and with breathing oxygen *(17)*. Holling and Venner *(18)* found that the level of pulmonary arterial pressure was more closely related to the level of disability than any other hæmodynamic measurement

Pulmonary vascular resistance may be expressed as units from the equation:

$$\frac{\text{mean P A. pressure} - \text{mean L A pressure}}{\text{cardiac output (L/min.)}}$$

(4) or as units of force (dynes sec./cm.^{5}) as described by Gorlin and Gorlin *(19)*. It is raised in mitral stenosis from levels below 2 units to 20–25 units because of organic and functional changes in the small arteries of the lung. Evans and Short *(20)* have shown that pulmonary hypertension in mitral stenosis is always associated with a reduction in the pulmonary arterial bed by structural changes affecting arterioles and small pulmonary arteries throughout the

lungs The vessels are constricted and undistensible, and are the seat of intimal proliferation Foci of medial hypoplasia or aplasia are common, and these deficiencies are thought to provoke proliferation in the presence of hypertension. In spite of these structural changes there is much evidence of a reversible functional mechanism as well. Certain ganglion blocking drugs, acetylcholine (*21*, *22*, *23*, *24*) and successful valvotomy (*4*, *25*) result in a fall of pulmonary vascular resistance, even in patients with an extremely high resistance. A fall in resistance from acetylcholine leads to a rise in left atrial pressure without significant changes in cardiac output, blood pressure or pulse rate Pulmonary vascular resistance probably increases with effort in some patients, and when the resistance is high, effort may cause a disproportionately great rise in pulmonary artery pressure. High pulmonary vascular resistance is positively correlated with severe pulmonary hypertension, low cardiac output, a relatively low arterial oxygen saturation and congestive heart failure A high pulmonary vascular resistance is only found in patients with severe stenosis

In pure mitral incompetence it is uncommon for the pulmonary artery pressure or the pulmonary [illegible]
However, in some patients with [illegible]
some *stenosis*, the resistance [illegible]
atrial pressure curves show a rapidly rising systolic wave and a rapid collapse to near normal diastolic levels Left atrial and left ventricular pressure curves taken at mitral valvotomy and compared with the amount of incompetence found by the surgeon, showed that the height of the "v" wave, the v-c difference, and the Ry/v ratio *were not* helpful in recognising incompetence, a so-called "correlated x descent" of over 5 mm Hg indicated mitral incompetence (*16*) Dye dilution curves provide valuable evidence concerning the presence and degree of incompetence (*26*, *27*, *28*) The appearance time of dye is shortened and the spread of dye particles is increased for any given cardiac output and volume. Korner and Shillingford do not claim that small amounts of regurgitation may be detected, but the method can separate those who clinically and surgically had little or no regurgitation from those with moderate or great regurgitation (*29*).

It must be emphasised that the correct assessment of the severity of mitral stenosis, the degree of associated [illegible]
combined [illegible]
clini[illegible]
dyn[illegible]

THE PRINCIPAL FEATURES OF PURE MITRAL STENOSIS CONTRASTED WITH THOSE FOUND IN PURE MITRAL INCOMPETENCE
(Brigden and Leatham, 1953. *Brit. Heart J.*)

	MITRAL STENOSIS	MITRAL INCOMPETENCE
Sex	Female preponderance	Male preponderance
History of rheumatic fever, etc.	Over half cases	Uncommon
Bacterial endocarditis	Rare	Common
Heart failure	Common	Late
Pulse	Small	Normal or increased
Apex beat	Palpable first sound	Suggests left ventricular hypertrophy
First sound	Loud	Normal
Second sound	Normal at apex	Inaudible at apex being included in systolic murmur
Opening snap	Frequent	Absent
Third sound	Infrequent	Frequent, often loud
Murmurs	Mid-diastolic } Presystolic } + or − thrill	Systolic, loud, long may be maximal in late systole (+ or − thrill)
X-rays		
Enlargement of left auricle	All degrees	All degrees—usually slight or moderate
Systolic backward movement of left auricle	Frequent	Frequent
Systolic expansion of left auricle (as shown by obvious left auricular pulsation in all views)	Never	Essential for X-ray ✓ diagnosis
Electrocardiogram		
P wave	Frequently large and bifid	Normal
Ventricular preponderance	Tendency to right	Tendency to left

MITRAL STENOSIS

Symptoms. *Dyspnœa on effort* is the commonest symptom. It is a good guide to severity of the mitral obstruction (*4, 30, 31*) and is closely associated with pulmonary venous congestion and increased stiffness (or reduced compliance) of the lung (*32, 33, 34*). In patients with significant dyspnœa, there is radiologically detectable pulmonary venous congestion and a mean left atrial pressure above 10 mm. Hg (*4*).

Orthopnœa, paroxysmal cardiac dyspnœa and pulmonary œdema are grades of dyspnœa occurring at rest and result from the same mechanism Attacks of pulmonary œdema may be precipitated by changes in rhythm, emotional disturbance, pregnancy and intercurrent infection The pulmonary capillary pressure may be low at rest, but rises steeply on effort in this group (5, 35, see p 102). Stenosis is usually of mild to moderate degree and pulmonary vascular resistance is not high Wood (4) found that 78% of patients with a really high vascular resistance had never had orthopnœa or paroxysmal dyspnœa

Cough is often due to chronic or *recurrent bronchitis which is* probably related to chronic pulmonary vascular congestion, though not necessarily related to its severity Parenchymatous lung disease in mitral stenosis is frequently responsible for further incapacity but rarely causes cor pulmonale: it is occasionally more important than the valve disease Some improvement in recurrent bronchitis occurs after operation

Hæmoptysis Five kinds are recognised (4). (i) sudden profuse pulmonary hæmorrhage, (ii) blood staining associated with attacks of dyspnœa due to acute pulmonary venous congestion, (iii) blood streaking with winter bronchitis, (iv) pink frothy sputum with acute pulmonary œdema, and (v) hæmoptysis due to pulmonary infarction It is probable that the massive type of pulmonary apoplexy is of venous origin occurring when left atrial pressure has risen suddenly in patients with a relatively low vascular resistance It is often an early symptom, the average time of onset being only one year after effort dyspnœa It is not considered to be a serious symptom, though often recurrent and often precipitated by pregnancy Some authors have considered that it may equally [illegible]

[illegible] operation.

Pain in the chest in mitral stenosis is not a prominent feature, but there are three types a submammary discomfort which may be psychogenic, and due to anxiety about the heart condition, a dull precordial discomfort when there is great cardiac enlargement, and true ischæmic cardiac pain (angina pectoris) which is due to failure of the coronary circulation when there is a low cardiac output from severe stenosis and *pulmonary* hypertension aggravated by anoxæmia Most patients, however, do not complain of pain.

Dysphagia is not an uncommon symptom (especially in the

combined lesion) and this is often associated with a dry persistent cough, or hoarseness of the voice from pressure on adjacent mediastinal structures by an enlarged left auricle. *Very rarely aneurysmal* enlargement of the left auricle appears to be the cause of erosion of the vertebral bodies, giving rise to severe pain between the scapulæ

Physical signs. In mitral stenosis these may be related to the anatomical abnormality of the valve and to the hæmodynamic derangements which result from the obstruction (see p 100). The

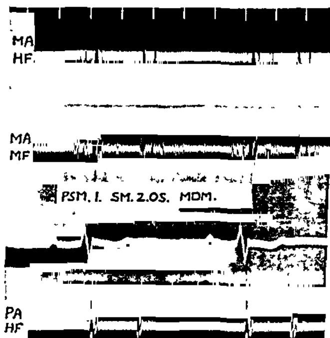


FIG 32. Mild mitral stenosis Phonocardiogram shows presystolic murmur (P S M), moderately loud first sound at the mitral area (M A), an opening snap (O S) seen best in high frequency record at the mitral area (H F M A) and diminuendo mitral diastolic murmur (M.D M)

mitral facies is due to peripheral vaso-constriction associated with a low relatively fixed cardiac output, together with a tendency to arterial anoxæmia. There is often a slight bulging in the left precordium, the cardiac impulse may be seen in the parasternal intercostal spaces (right ventricle) and the apex beat (left ventricle) ... separate pulsation further to the left On palpation, the
...oping quality, largely due
1 An apical diastolic or

presystolic thrill is common and its presence depends on the loudness of the characteristic murmur Over the parasternal region there may be a strong pulsation due to right ventricular hypertrophy, indicating pulmonary hypertension, which is also suggested by a palpable pulmonary closure over the pulmonary artery

Auscultation provides the most valuable evidence in patients with mitral stenosis The first sound is loud, and on the phonocardiogram it is late when compared with the QRS (Figs. 32 and 33)

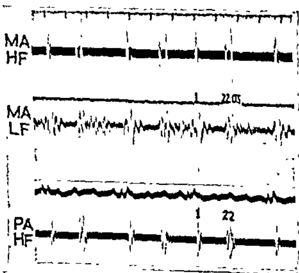


FIG 33 Severe mitral stenosis An early opening snap (O S) is seen after the two second *sounds* (22) There is a long mid diastolic murmur on the low frequency *record* (L F) and there is atrial fibrillation

When the f

... loudness is concerned partly with severity and partly ... movement of with cusp mobility

The intensity of the pulmonary second sound is increased by pulmonary hypertension, when tension is high and the artery dilated, there may be an ejection click in early systole and the second sound is sometimes followed by the murmur of pulmonary incompetence *The opening snap* occurs in early diastole between

0·03 sec. and 0·14 sec after the beginning of the second sounds, the interval between the two second sounds being between 0 01 and 0 05 sec. (Figs. 32 and 33). It is heard best inside and above the apex and is higher pitched and earlier than the third heart sound (*37*). Its presence usually indicates a pliable valve with significant stenosis; it is thus a most valuable sign. There is a positive correlation between intensity of the first heart sound and intensity of the snap. The following factors are associated with a soft first sound in mitral

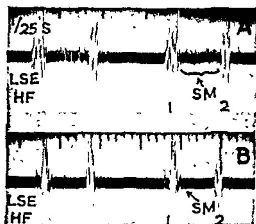


FIG 34. Phonocardiograms showing a pan-systolic murmur present durin
petence (A),
made at left
filter (H F)

valve disease and with the absence of an opening snap. (i) calcification at the mitral valve with or without evidence of significant mitral incompetence, (ii) dominant mitral incompetence, (iii) a very high pulmonary vascular resistance The "snap" may also be absent when there is a massive left atrial thrombus, and, rarely, when there is co-existent aortic valve disease .

There is a rough positive correlation between lateness of the first sound and earliness of the opening snap with the severity of the mitral obstruction, thus a very early snap is associated with tight stenosis, and a late one with mild stenosis The third heart sound
! with rapid
ird sound is
associated with

MURMURS. An apical *pan-systolic* murmur is a reliable guide to the presence of mitral incompetence in the presence of stenosis (*38*),

provided that it is not mistaken for a tricuspid incompetence murmur heard unusually far to the left (Fig. 34). This difficulty diminishes if due regard is paid to exact distribution of the murmur and its variation with respiration Conversely, the absence of a pan-systolic murmur is a reasonably good guide to the absence of mitral incompetence (4) A soft mitral pan-systolic murmur is more common in patients with severe stenosis when there is atrial fibrillation The *mitral diastolic murmur* is long in all severe cases of stenosis, intensity seems to bear little relation to orifice size, but in patients with a very high pulmonary resistance (usually having severe stenosis), the murmur may be very soft and at times even absent (39)

ATRIAL FIBRILLATION is common when there is associated incompetence, it brings deterioration in the cardiac status of patients with mitral stenosis Its onset may precipitate paroxysmal dyspnœa, and ...

... becomes larger after atrial fibrillation, the cardiac output tends to be lower (4) The risk of systemic embolism is greater in patients with atrial fibrillation than in those with normal rhythm.

Systemic hypertension is no more common in mitral stenosis than in normal controls of the same age and sex (40) 3% of 300 cases had blood pressures of 160/100 or more (4)

The electrocardiogram. (Figs 35 and 36) The P wave is abnormal in all cases of severe stenosis It is widened (up to 0 12 sec in severe grades) and notched or bifid The two components reflect right and left atrial activity, separated by 0 05 sec compared with 0 03 sec in controls (41) This bifid P wave is ...

...

Right ventricular hypertrophy is related to the severity and duration of pulmonary hypertension It probably never occurs until the pulmonary vascular resistance commences to rise Right ventricular preponderance is found increasingly often as the mitral valve reaches its smallest size (5). The pattern of right bundle branch block mostly indicates right ventr... ...pertrophy in mitral ...

... the electro-
...ly dominant mitral stenosis demands a

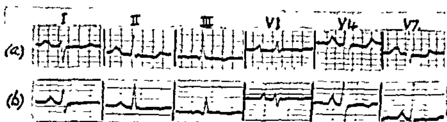


FIG. 35 *Mitral stenosis with moderately high pulmonary* vascular resistance. (*a*) Before valvotomy, showing bifid P waves and moderate right ventricular hypertrophy (*b*) One *year after valvotomy: left atrial component of P is less.* Increased RI and RV7 with deeper SV1 indicates less right ventricular hypertrophy.

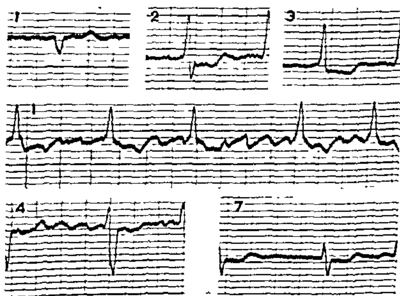


FIG 36 Mitral stenosis with high pulmonary vascular resistance showing monophasic R waves in CR1 (middle row), the coarse "f" waves of atrial fibrillation are shown best in this lead.

further search for the presence of mitral incompetence or aortic ... systemic hypertension.

... tral stenosis are well ... s of severe stenosis.

The pulmonary artery and its secondary branches are enlarged when there is pulmonary hypertension whilst the peripheral branches are narrowed, especially at the bases of the lungs (43). Pulmonary venous congestion is largely responsible for the hilar congestion

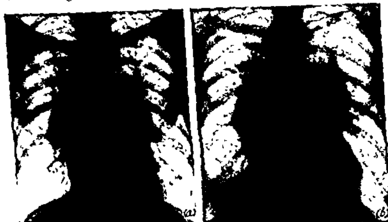


FIG 37 Mitral stenosis with high pulmonary vascular resistance (a) There is intense pulmonary venous congestion and the rhythm is regular; (b) After the onset of atrial fibrillation there is some increase in heart size and further venous congestion

seen in severe stenosis It is usually proportioned to the degree of dyspnœa, but there are occasional anomalies The vast majority of patients with pulmonary venous congestion have left atrial pressures between 10 and 30 mm Hg (4) Short horizontal lines (Kerley's lines) appear in basal regions and are related to chronic congestion These septal lines are present in 75% of patients with tight mitral stenosis (Fig. 37).

The left atrium is characteristically enlarged, but associated mitral incompetence produces even greater enlargement Occasionally a giant left atrium is associated with pure stenosis In patients

the extent of right ventricular enlargement from the general cardiomegaly. The right atrium may be moderately enlarged but when it is so, the probable cause is tricuspid valve disease.

Calcification of the mitral valve is common and may be detected by radioscopy, image intensification or tomography. It should always be sought when surgery is considered. Mitral incompetence is much more common in patients with gross calcification than those without (*44*). Some authors deny this (*5*) Thin linear calcification forming part of the atrial circumference indicates organised clot.

Hæmosiderosis shows a close relation to severe hæmoptysis and is considered to be due to multiple hæmorrhages from bronchopulmonary anastomosis (*45, 4*).

Surgical treatment. Valvotomy for mitral stenosis has now been established for ten years, but the first attempts at surgical treatment were made more than thirty years ago by Souttar (*52*), and Cutler and Beck (*53*).

Mitral valvotomy is indicated when obstruction to blood flow at the mitral valve is the dominant disorder and of sufficient degree to cause symptoms. Success after operation is largely determined by the effectiveness of relief of this obstruction. In most patients selection for operation may be made by clinical assessment aided by electrocardiography and radiology.

Since a close correlation exists between the degree of breathlessness on effort and the size of the mitral orifice, effort dyspnœa, orthopnœa and cardiac asthma are the most important indications Completely asymptomatic patients may live normal lives and do not need treatment, but operation should be performed on all patients with "pure" mitral stenosis who have dyspnœa on effort In those with very mild non-progressive symptoms operation may be deferred or determined by consideration of social, economic and psychological factors. On the other hand, valvotomy is urgent when symptoms are clearly progressive; such patients should not be allowed to deteriorate to the status of complete cardiac invalidism, but even at this level when there is chronic failure, operation may produce remarkable improvement. Pulmonary œdema is an urgent indication for surgery, so is repeated hæmoptysis. There is evidence that operation diminishes the late risk of further systemic embolism in patients who have already had one episode, so that embolism is an added reason for valvotomy, but the operative risk in such patients is somewhat greater.

Objective evidence pointing to surgically significant stenosis includes a loud first sound and loud opening snap, a long mitral

diastolic murmur, electrocardiographic evidence of right ventricular hypertrophy and "P mitrale," radiological evidence of pulmonary venous congestion, and left atrial enlargement. In a small number of cases where signs and symptoms are equivocal, hæmodynamic studies are indicated. Raised pulmonary capillary pressures indicate raised left atrial pressure, the form of the pulmonary "capillary" pulse tracing may be used to calculate the Ry/v ratio. Left atrial and left ventricular catheterisation by percutaneous route to determine the gradient across the valve, is rarely, if ever, indicated.

Operation is contra-indicated by serious mitral incompetence and serious aortic incompetence, but minor degrees are acceptable if the left ventricle does not reveal clinical, radiological and electrocardiographic evidence of enlargement. Mild degrees of mitral incompetence may even be improved after valvotomy, especially if the cusps are mobile (*51, 55*), when combined with aortic valvotomy, the results are good (*vide* p. 127)

Pulmonary hypertension, due to a significantly raised pulmonary vascular resistance, does not contra-indicate operation. The pulmonary artery pressure falls after operation even in patients with extremely high pulmonary vascular resistance (*54, 25*). Atrial fibrillation does not contra-indicate operation, but overall results are not so good. *Calcification* of the mitral valve is not a contra-indication, but if it is extensive it is unlikely that a good result will be achieved (*54, 31*), especially when there is associated incompetence.

Rheumatic activity is an indication to postpone operation, but if life is threatened by the severity of the obstruction delay should be avoided. It is even possible that improvement of circulatory dynamics may aid the regression of the carditis. The assessment of the rheumatic activity is often difficult, as the usual criteria are mostly absent in patients with stenosis severe enough to warrant surgery. The problems concerning rheumatic activity and valvotomy are unsettled and there are divergent views. There is certainly little or no correlation between Aschoff nodes found in atrial biopsies and the clinical course of these patients. Parenchymatous disease of the lung in the form of bronchitis and emphysema does not contra-indicate operation, but results depend on the relative dominance of the cardiac or pulmonary disease. The risks of operation are obviously increased.

Pregnancy is no bar to mitral valvotomy, but it is obvious that most clinicians would advise postponement of operation unless there are urgent indications, such as increasing paroxysmal dyspnœa in

spite of treatment, or an attack of pulmonary œdema. The risks of operation are probably no greater in the first trimester, but thereafter the risk is increased and operation should only be performed if it is clear that medical treatment is not preventing deterioration after a thorough assessment of all possible factors. In the vast majority of cases it is possible to carry women with heart disease through pregnancy (*56*), but this depends on many factors including good co-operation of the patient, and availability of social services in the community. *Burwell considers that surgery is almost never* necessary. However, in the great majority of reported cases of valvotomy the result has been satisfactory

RESULTS OF MITRAL VALVOTOMY The dominant factor in determining clinical improvement is the effectiveness of relieving obstruction at the mitral valve, but even when function is greatly improved the anatomical state of a grossly deformed valve is clearly *not returned to normal (31, 57, 58)*

The overall mortality is 5–6% but for most suitable patients with small hearts, sinus rhythm and pure stenosis the risk is not greater than 1%. Most studies have shown that some 70% of patients are improved by operation and in the majority of patients improvement has been maintained (Fig. 35). Poor results and regression are due to inadequate operations, pre-existing serious lung disease, gross calcification of the valve, myocardial disease, traumatic mitral incompetence and rarely, refusion of commissures

Post-operative atrial fibrillation is common Spontaneous conversion to sinus rhythm may occur within fourteen days after the operation, if atrial fibrillation persists quinidine should be given between the tenth and fourteenth post-operative day Successful conversion is unlikely before

THE POST-OPERATIVE PYREXIAL SYNDROME (*60, 61*) is characterised by some of the following features fever, chest pain, pericardial friction, a rise in jugular venous pressure, slight œdema, an *increase* in size of the heart shadow and rarely arthralgia Non-specific laboratory evidence of inflammation may be present Some 10–20% of patients show some features either early or late in the post-operative period. For the vast majority of patients the condition is not serious and merely delays convalescence for two or three weeks; a few deaths from heart failure have been reported (*62*), but in such cases it seems likely that rheumatic activity was the

The cause of the post-valvotomy syndrome is uncertain, but it appears to be an unusual accentuation, persistence and recurrence of local traumatic sequelæ, perhaps an unusual reaction of rheumatic subjects to blood in the pericardial sac. It is probably not due to rheumatic activity owing to the absence of fresh streptococcal infection, absence of arthropathy or nodules, carditis and a response to salicylates However, there are occasional patients who show clear evidence of a recurrence of rheumatic fever from which the post-valvotomy syndrome should be differentiated.

MITRAL INCOMPETENCE

Pure chronic organic mitral incompetence in adults is not as common as other forms of mitral valve disease but has some distinctive features Application of the clinical features of pure incompetence to the findings in mixed lesions aids in assessment of the degree of associated incompetence

In contrast to mitral stenosis, males preponderate Only 25% give a history of past rheumatic fever, and superimposed bacterial

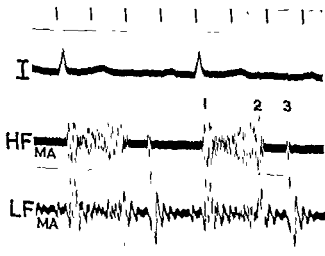


FIG 38 Mitral incompetence Phonocardiogram shows a long systolic murmur with crescendo in late systole The second sound (aortic) is included in the murmur at the apex (M A) in the high frequency recording (H F) but can be seen in the low frequency record (L F.) The third sound is clearly seen

endocarditis is common. Ectopic beats, associated with a hyperkinetic ventricle are common when there is more than mild incompetence; palpitation results. Unusual fatigue is more prominent than dyspnœa.

SIGNS. The pulse is normal or jerky, having a quick up-stroke with a "small water hammer" quality (4). When incompetence is of moderate to severe degree, the apex beat reveals left ventricular enlargement and an early diastolic filling wave may be seen and felt (6). *Auscultation* provides the best evidence of mitral incompetence and there is general unanimity concerning the following points The first sound is normal or soft, it is followed by a pan-systolic murmur which is loudest at the apex and here the aortic second sound may be "buried in the end vibrations of the murmur," so that it becomes inaudible. In mild cases the murmur has a crescendo quality and has been mistaken for an innocent late systolic murmur (see Fig. 38). Ventricular septal defects may produce a pan-systolic murmur which is, however, loudest at the left sternal edge. When mitral incompetence is more than slight, *there is a third heart sound. An opening snap is absent.*

RADIOLOGY. The presence of expansile pulsation of left atrium is a good sign of considerable mitral reflux, but its absence is compatible with mild to moderate degrees of incompetence. Systolic expansion of the left atrium must be distinguished from a jerky backward displacement which may occur in mitral valve stenosis. This sign is best seen in the antero-posterior view on radioscopy, when both left and right upper borders of the heart shadow, formed by the left atrium, move outwards as the apical region of the ventricle moves in with systole · In contrast to mitral stenosis, hilar con- [illegible] the P wave may be a [illegible] ly present. The QRS complexes show a tendency to left ventricular preponderance but the degree of change is normally slight and rarely reaches the severity found in systemic hypertension or aortic valve disease.

Treatment. The majority of patients with mild to moderate pure mitral incompetence have a reasonable life expectancy, but bacterial endocarditis is a real hazard (6) and prophylactic penicillin is indicated when there is risk of infection

The surgical repair of mitral incompetence has been unsatisfactory so far. Various methods, including the use of vein or pericardial grafts (46, 47), artificial valves (48, 49, 50), and the suturing of leaflets have been tried. Perhaps the most attractive and satisfactory

method so far is the use of a total circumferential purse string suture to narrow the left atrial-ventricular ring (*51*); the orifice which the pathological valves have to occlude is narrowed. Glover and Davila (*51*) report the results in 12 cases with advanced, almost

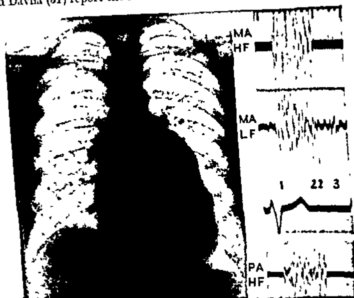


Fig 39 Mitral incompetence X-ray shows unusually large

(22, 3)

terminal disease prior to operation The high mortality was not surprising in view of the severity of the disease Four were living in an improved state Their results clearly point the way It is certain that great improvement would follow the significant reduction of mitral incompetence in patients whose left ventricular myocardium was not severely damaged

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TRICUSPID VALVE DISEASE

Rheumatic tricuspid valve disease is almost always associated with mitral or aortic valvulitis. The tricuspid valve is affected at necropsy examination in approximately 20% of patients with mitral stenosis when minor degrees of rheumatic inflammation are included (*1*, *2*) but only some 8–9% show definite evidence of stenosis (*2*, *3*) a higher figure (11%) is given by Soulié *et al.* (*4*), but Wood (*5*) found that only 3 3% of a series of cases of mitral stenosis had clinical evidence of significant tricuspid stenosis and this is more in line with the experience of cardiologists Some measure of tricuspid incompetence is associated with almost all cases of tricuspid stenosis (*11*)

Rare causes of organic acquired tricuspid valve disease are disseminated lupus erythematosus (see p 160), argentaffin carcinoma and endomyocardial fibrosis (see p 162).

Tricuspid stenosis. The main features of this condition have been known for a long time, but the surgical treatment of mitral stenosis and the introduction of hæmodynamic methods has stimulated a reinvestigation of the clinical features of this condition which is almost always associated with a severer degree of mitral stenosis (*3*, *6*, *7*, *8*, *9*)

Obstruction at the tricuspid valve prevents the rapid equalisation of atrial and ventricular pressure, hence a pressure gradient develops across the valve which may be recognised by cardiac catheterisation In severe cases it appears that these pressures may not equalise

Contributions by Gibson and Wood (*6*) and Yu *et al* (*7*) are substantially similar, they find that a confident diagnosis can be made when the following features are present. (1) Absence of symptoms of pulmonary venous congestion (chronic œdema and

ascites are only seen in advanced cases). (2) A high venous pressure in the absence of a high pulmonary vascular resistance, pericardial effusion, uncontrolled auricular fibrillation, or severe mitral incompetence. (3) A venous pulse showing a giant "a" wave in cases with normal rhythm, and a gentle "y" descent without a properly defined "y" trough in those with auricular fibrillation (4) A quiet right ventricle and unimpressive pulmonary second sound. (5) A diastolic or presystolic murmur at the tricuspid area, waxing on inspiration (6) An opening snap at the left sternal edge in the presence of calcific mitral stenosis. (7) A tall right atrial P wave in the absence of electrocardiographic evidence of right-ventricular hypertrophy (lead V1, or CR1). (8) Disproportionate dilatation of the right atrium without enlargement of the pulmonary artery and with relatively little pulmonary venous congestion

The exaggerated presystolic wave in the jugular venous pulse in tricuspid stenosis was recognised by Mackenzie, but these sharp waves may also occur in conditions with a great increase in right ventricular pressure: in particular "a" waves associated with pulmonary hypertension in mitral stenosis (as noted in (2) above) cause difficulty in differential diagnosis *(8)*; however, there is usually an early diastolic collapse of the jugular pulse, whereas in tricuspid stenosis the obstruction leads to a slower "y" descent The opening snap in mitral stenosis is usually well heard at the left sternal edge *(10)*, and it is the experience of many physicians that this sound may be heard even in the right chest, so that it is obviously difficult to be certain whether this sign arises in the right or left atrio-ventricular valve The qualification imposed by Gibson and Wood *(6)* is not absolute, namely that this sound is a sign of tricuspid stenosis when the mitral valve is calcified, as in some cases of calcific mitral stenosis a soft snap may be heard from that valve

The clinical features ultimately depend on the relative degree of tricuspid stenosis and mitral stenosis A severe degree of obstruction at either valve may largely mask the symptoms and signs produced by the less severely affected valve

Tricuspid valvotomy. Anatomical study of diseased tricuspid valves shows that there is almost always incompetence even when the stenosis is tight *(11)* It is obviously important to avoid causing more incompetence by operation, and in most cases only a limited valvotomy is indicated. Bailey *(12)* advised against division of the antero-medial commissure because the production of incompetence is likely with a full valvotomy Many operations for tricuspid stenosis have now been performed. Bailey and Bolton *(13)* explored

the valve in 98 cases of mitral valvotomy and found tricuspid stenosis in 15 Hollman (*11*) noted reports of 18 patients who had undergone valvotomy, and added one whose dominant symptom ... angina pectoris which was relieved by tricuspid and mitral

Tricuspid incompetence. Tricuspid incompetence is mostly functional and due to dilatation of the valve ring and the right ventricle It is inevitably associated with the development of heart failure, it may be due to organic disease of the valve and is then often associated with some degree of stenosis. The recognition of

liver

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2 Smith, J A, Levine, S. A 1942 *Amer Heart J.* 23, 739
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13 Bailey, C P, Bolton, H E 1956. *N Y. St J Med* 56, 825
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AORTIC STENOSIS

The recognition and assessment of severity of aortic stenosis is especially important now that surgical relief of the obstruction is possible Cicatricial narrowing of the aortic valve is common, and clearly the result of rheumatism when it is combined with mitral valve disease in an adult the lesion is isolated in some 25–35% (*1*) of all patients with aortic stenosis

Clinical and pathological investigation has not solved the old problem of the cause of calcific stenosis in adults The high average

age of death, the low incidence of a history of clinical rheumatism and the presence of calcification suggest a degenerative ætiology, but do not exclude rheumatism as the identical lesion is frequently associated with mitral valve disease The balance of evidence points to a rheumatic origin in most cases (2), but little is to be gained from a solution to this problem. More importance must be attached to the possibility that a reasonable proportion of cases of calcific aortic stenosis are of congenital origin (see p. 47). It is not uncommon for aortic valve deformities associated with coarctation of the aorta to become calcified and stenosed (see p 67).

The movement of healthy and diseased aortic valves has been studied by cinematography (3) By such methods the greatly diminished movement, obstruction and inefficiency of the valves in calcific aortic stenosis may be clearly seen. The valve lumen is triangular in health, and it becomes a small distorted triangle in disease (3, 4) The important pathological feature of aortic stenosis *from the practical point of view is its great tendency to calcification* (5). There are all grades of stenosis and deformity, depending on the extent of fusion of commissures and the amount of calcification (4)

The left ventricle is hypertrophied to a degree which depends on the severity of stenosis, the presence of coronary disease and presumably on the length of survival Occasionally the heart weighs over 1000 G but the average is 600 G (6). Patchy fibrosis is usual, but large homogeneous areas of damage due to extensive infarction are uncommon Coronary arteries are more commonly affected by occlusive disease than has been generally stated. In eleven patients dying suddenly with proven aortic stenosis, nine had severe stenosis but three had severe coronary atherosclerosis (6)

HÆMODYNAMICS. The *gradient across the valve* is measured by simultaneous electromanometric recording of brachial arterial pressure and intraventricular pressures The intraventricular pressure may be obtained by percutaneous introduction of a needle into the left atrium, into which a fine catheter is inserted via the needle, and advanced to the ventricle (7) Direct percutaneous puncture of the left ventricle appears to be a safe and more satisfactory method (8, 9, 5)

It is probable that cardiac output is maintained within normal limits until late in the natural history of aortic stenosis This is attained by increased work of the left ventricle, when obstruction is severe, intraventricular systolic pressures of 300 mm Hg and more are not uncommon and result in aortic systolic pressures of only

100–150 mm. Hg In late stages of the disease the end diastolic pressure in the left ventricle is elevated to 20 or 25 mm. Hg

Obstruction to the left ventricular outflow causes prolongation of the total ejection period which is appreciated as the slow_rising pulse The time of the up-stroke may be measured on arterial pulse pressure curves and is prolonged to 0 15 sec. or more (*10*) When an arterial oscillographic method is used with a neck cuff to show the regional changes in the pressure pulse form (*11*), the first half of the up-stroke time is prolonged from a normal range of 0 04–0 06 sec. to 0 05–0 14 sec The pulse wave form is only roughly related to severity of stenosis, numerous other factors such as stroke output, left ventricular performance, aortic incompetence, elasticity of the great vessels and peripheral resistance influence the pulse contour It follows that no single pressure measurement and record can be used as an index of severity

The normal aortic orifice at the valve ring is approximately 3 sq cm It seems that this area must be reduced by more than 75% to reach a critical size of 0 5–0·7 sq cm before aortic stenosis produces significant clinical symptoms, in combined aortic stenosis and aortic incompetence, however, the critical size is larger, being approximately 1 5 cm (*12*, *13*)

Clinical Features

A male preponderance of approximately 3 to 1 (the reason for which is unknown) has been confirmed in many recent studies In contrast to mitral stenosis, patients with aortic stenosis often live a long symptom-free life, but from the time that symptoms appear deterioration tends to be rapid and death often occurs within two years

Any of the following symptoms may appear alone or in combination with others, abnormal fatigue, angina pectoris, dizziness and syncope, and breathlessness from left ventricular failure

... and the reduced supply from a low coronary perfusion pressure due to the aortic stenosis, and possibly still further reduced by coronary atheroma Although a serious symptom, often indicating a prognosis of less than two years, a few patients may survive as long as fifteen years with effort pain (*6*) Nocturnal attacks are common Some patients have prolonged attacks of pain and it is probable that some degree of local myocardial death is

sustained in these attacks. There is a much greater incidence of coronary atheroma in aortic stenosis patients with angina than in those without (40% versus 13·8%) (*6*). Sudden death is more common in patients with angina.

SYNCOPE (and its minor equivalent of dizziness) is common in isolated aortic stenosis, varying from 5 to 25% in different series Angina is more common in patients with syncope than in those without (75% versus 23%), and this is presumably due to the fact that both are symptoms of severe stenosis Syncope is characteristically related to effort (14 of 16 cases in one series (*15*)) Various mechanisms have been suggested, including hypersensitive carotid sinus, cerebro-vascular disease and arrhythmia, but there is no evidence that these play any part in the usual form of effort syncope. It is probable that the ventricle is unable to elevate its output sufficiently (and in this sense it is failing) in the presence of peripheral vasodilatation (in contrast to mitral stenosis, the stimulus to peripheral constriction from pulmonary venous congestion is largely absent), acute hypotension results and the usual pattern of vaso-vagal syncope with bradycardia follows. Syncope is occasionally due to arrhythmia, e g. heart block, but then it is unrelated to effort.

Physical signs. These are well known and follow from the hæmodynamics of aortic obstruction. Left ventricular enlargement is of the hypertensive rather than the hyperkinetic type, and may be felt as a heave at the apex when severe The murmur is characteristically heard best at the left sternal edge and aortic area It is maximal in mid-systole (*16*) and sometimes preceded by an ejection click (Fig. 40) A thrill is clearly only present when the murmur is a loud one When aortic stenosis is combined with incompetence, and there is probably some incompetence in most apparently "pure" cases of aortic stenosis, a soft early diastolic murmur may be heard When there is great left ventricular hypertrophy or left bundle branch block, the normal tendency to increased splitting of the second sounds on inspiration is reversed, due to delay of the aortic component beyond the time of pulmonary valve closure

An anacrotic pulse may be felt when stenosis is moderate to severe. A bisferiens pulse showing recession of pressure in the middle of the pulse wave appears when there is significant combined aortic incompetence· this may be due to a "Venturi" effect (*17*) The frequency of arrhythmia varies in different series. Atrial fibrillation is common when aortic stenosis is mixed with mitral valve disease, but occurs in perhaps only 10% of pure cases, and is then a grave prognostic sign

advance" (13)

THE ELECTROCARDIOGRAM provides valuable evidence of the state of the left ventricle It is normal in only the milder cases, and the degree of change bears a rough relation to severity There is, however, no very constant pattern of abnormality apart from the clear

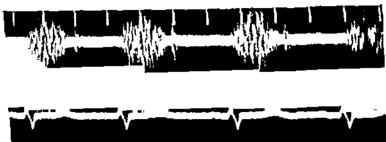


FIG 40 Aortic stenosis Phonocardiogram shows diamond-shaped ejection systolic murmur ending before the aortic second sound

evidence of left ventricular damage, which appears in 70% as left ventricular preponderance, left ventricular strain or left bundle branch block

Treatment. Surgery is the only way of diminishing organic obstruction at the aortic valve and should be a serious consideration in every case of aortic stenosis Bailey *et al* (4) have reported 287 operations, Brock (5) has reported 120 operations, and many other reports have appeared recently The present surgical techniques carry an appreciable morbidity and mortality which are not acceptable for totally asymptomatic patients with mild to moderate aortic stenosis which may be compatible with a long life

failure indicates an inoperable state

but successful operation is possible after the development of left-sided failure if this has responded to medical treatment, and especially when an episode of left ventricular failure has been precipitated by infection. On physical examination a forceful left *ventricular apex beat and a slow rising pulse* mostly point to a severe obstruction. An aortic diastolic murmur in the absence of other evidence of a large leak does not contra-indicate surgery but probably increases the risk.

A normal *electrocardiogram* is not compatible with stenosis of the severity to justify surgery On the other hand, deterioration in electrocardiographic signs of left ventricular damage is an added reason for surgery. Calcification seen at the valve on radioscopy is not a contra-indication but it reduces the probability of a first-class result (*5*). It is clearly preferable to operate before calcification develops, this is rarely possible in adults

In many patients operation can be advised without recourse to tests designed to establish pressures on each side of the obstruction: in any case, aortic and intraventricular pressures may be, and should be, determined at operation before the valvotomy. In other cases further tests for pre-operative assessment are necessary Simultaneous percutaneous left ventricular puncture and brachial artery puncture seem to be the most satisfactory pre-operative method of obtaining the pressure gradient, which should not be less than 50 mm. Hg if surgery is contemplated.

Brock (*5*), with much evidence to support his view, considers that pressure records at operation are reliable and comparable with those taken beforehand, especially if regard is paid to the state of ventricular action at operation Complete abolition of the gradient is often not possible but in obtaining a residual gradient of 30–50 *mm Hg, symptoms may be relieved and prognosis greatly* improved.

Surgical approach. It is clear that blind techniques are bound to be unsatisfactory compared with open direct-vision valvotomy Bailey (*18*) described the technique of passing a valvulotome through the left ventricle to the valve which was split by an expanding dilator This technique, although abandoned by Bailey and other American surgeons in favour of a trans-aortic approach, has been used and developed by others including Brock, who has used it for most of his cases. Both methods produce improvement in approximately 70% of patients, and the operative mortality should not be more than 10 to 15%. The immediate operative mortality of the trans-ventricular route is probably twice that of the trans-aortic

(4), but the number of late deaths, average time of their occurrence and the post-operative clinical response makes the two procedures of equal value

It is clear that open direct-vision operation will largely replace blind techniques in the future. Several surgeons performed open aortic valvotomy using a pump oxygenator system or hypothermia early in 1956 (5) In Bailey's series of 11 cases there was one death and all survivors were considerably improved clinically, and none developed *aortic incompetence* (4). This method is advocated for all operative cases of congenital aortic stenosis and for others with extensive calcification of the valve The problem really concerns the development of a relatively simple safe technique of managing the open arrested heart so that all cases may be done under direct vision

COMBINED AORTIC AND MITRAL VALVOTOMY. *Aortic stenosis should* be relieved in most patients where mitral valvotomy is indicated for co existing mitral stenosis Increased flow through a widened mitral orifice causes increased load on a left ventricle already overloaded by obstruction The results for the double [illegible]

[illegible]

[illegible] valve indicates valvotomy (5)

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2 Karsner, H T, Koletsky, S 1947 *Calcific Disease of the Aortic Valve* J B Lippincott Co, Philadelphia
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8 Brock, R *et al* 1956 *Thorax*, 11, 163
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12 Gorlin, R *et al* 1955, *Amer J Med* 18, 855
13 Daley, R 1957 *Proc Roy Soc Med* 50, 817
14 Bergeron, J. *et al* 1954 *Arch int Med* 94, 911
15 Hammarsten, J 1951 *Arch int. Med* 87, 274
16 Leatham, A 1951 *Brit Heart J* 13, 153
17 Fleming, P 1957 *Brit Heart J* 19, 519
18 Bailey, C P, et al 1952 *J Amer med Ass* 150, 1647.

but successful operation is possible after the development of left-sided failure *if this has* responded to medical treatment, and especially when an episode of left ventricular failure has been precipitated by infection. On physical examination a forceful left ventricular apex beat and a slow rising pulse mostly point to a severe obstruction. An aortic diastolic murmur in the absence of other evidence of a large leak does not contra-indicate surgery but probably increases the risk

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greater value than elaborate measurements of films (5) The angiocardiographic signs are dilatation of ascending aorta above 38 mm, measured in the left anterior oblique position, irregularity of the lumen and variations in aortic wall thickness However, even with angiography similar changes can be [illegible] degenera[illegible] the asce[illegible] and it may be used as evidence of infection to outweigh the implications of negative serology (6)

The outcome of 61 patients with uncomplicated aortitis has been studied in patients having regular examinations for 3–14 years (7) Progression to aortic incompetence or further dilatation of the aorta [illegible] first but a third of those showing progression became abnormal

Aortic incompetence results from aortic dilatation and from affection of the valve cusps which become separated by swelling at the commissures and distorted by fibrosis. Routine examination of syphilitic patients has shown that a large number of patients with incompetence have no symptoms and remain well for years (2), it thus appears that prognosis is not so bad as in patients with symptoms of heart disease who formed the basis of the older impression that prognosis was always bad Probably some 50% are symptomless at the time of diagnosis (8) Angina pectoris occurs in about half the patients who appear with cardiac symptoms, the other symptoms and signs are the same as occur in other forms of aortic incompetence

Coronary ostial stenosis is the usual cause of cardiac pain in patients with cardiovascular syphilis It is particularly associated with aortic incompetence, presumably because [illegible] of ischaemia Angina of effort is the most common type of pain, but nocturnal attacks without paroxysmal dyspnœa are not uncommon (9) The presence or absence of cardiac ischæmia is probably the chief determinant in prognosis

Aneurysm Saccular and diffuse aneurysm, along with other manifestations of late syphilis, is slowly becoming less common. Diffuse or fusiform aneurysms merge into uncomplicated aortitis

CARDIOVASCULAR SYPHILIS

This disease is becoming less common in the British Isles because of social betterment, public education in venereology and effective early treatment of syphilis. Apart from the falling incidence of the primary disease, the incidence of cardiovascular damage in subsequent follow-up of treated primary cases has also fallen. Statistics concerning incidence of cardiovascular lesions are of limited value because there has been no general agreement on diagnostic criteria either clinically or at necropsy (*1*) In a recent report of 1330 syphilitic patients referred mostly before treatment for cardiac investigation, 15% had cardiovascular syphilis and 16% had other non-luetic cardiac abnormalities (*2*)

In a study of 749 patients, the incidence of cardiovascular syphilis was 14·1% amongst those doing heavy manual work. Whilst it was 8·7% in those doing sedentary work, so that occupation prior to onset of heart disease may be a factor The age of onset depends mainly on the age of primary infection. More than half of a large series had developed clinical signs and symptoms within twenty years of the initial infection (*4*). The incidence of neuro-syphilis in patients with cardiovascular syphilis is approximately 25% (*1*)

Clinical Features

Syphilitic aortitis is the only important condition from the cardiological point of view, since both syphilitic myocarditis and gumma of the heart are extremely rare. Syphilitic aortitis comprises (i) uncomplicated aortitis, (ii) coronary ostial stenosis, (iii) aortic incompetence, and (iv) aortic aneurysm (63% of 202 cases recognised at routine cardiological examinations (*2*)), whereas isolated aortitis is the rarest, presumably because of the paucity of signs Two useful points in the diagnosis of aortitis are the high frequency of a persistently raised sedimentation rate, and the common occurrence of thin streaks of calcification in the ascending aorta.

Uncomplicated aortitis rarely causes symptoms, though a dull substernal ache has been attributed to it A systolic murmur in the aortic area, and a rather loud musical quality of the aortic second sound in the absence of systemic hypertension may be significant (*5*). Diagnosis is more often made on radiological evidence (given positive laboratory evidence of luetic infection), and improved techniques have resulted in more frequent recognition, fluoroscopy in all positions by an experienced cardiologist or radiologist is of

prevents the Jarisch-Herxheimer reaction which is extremely rare in penicillin treatment of cardiovascular syphilis.

Penicillin is undoubtedly a safe agent in both complicated and uncomplicated aortitis and study of a large series of treated cases shows that it results in symptomatic improvement (*13, 14*). A history of penicillin sensitivity should always be sought, for this is a more serious problem than the Jarisch-Herxheimer reaction. A slight elevation of temperature during the first forty-eight hours of treatment is not uncommon.

Penicillin alone is used in many clinics. A survey by the World Health Organisation of current practice in 277 clinics showed that 65% of the participants used penicillin alone for syphilis in general (*14*). However, it would seem reasonable to follow penicillin with a course of weekly injections of bismuth (0.1 G) for ten to twelve weeks in the case of syphilitic aortitis.

There is no general agreement concerning the type of penicillin or dosage schedule, but a minimum total of 10 mega units is accepted. 600,000 units of procaine penicillin twice daily during ten days of bed rest is advised. The final evaluation of penicillin therapy in cardiovascular syphilis must await future histopathological study, and even when this is available, control series are likely to be inadequate.

Surgical treatment. A variety of techniques have been applied to aneurysms during the last few decades. No more than limited success can be expected having regard to the pathology of the material. Various methods of wiring aneurysms have been tried, and more recently the technique of wrapping in polythene cellophane has been used with some success (*15, 16, 17*). The cause of the fibrous tissue reaction appears to be the chemicals used in the manufacture of polythene, which should be impure to be effective. This method is most useful when applied to fusiform aneurysms (*16, 17*). Occasionally, when an aneurysm does not involve or approximate to main arterial trunks, resection and replacement with a graft is possible (*18, 19*).

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and are often associated with aortic incompetence which may give *some "protection" against the formation of a saccular aneurysm.* The male preponderance of aneurysm cases is well known, as are the other clinical features of morbid anatomy. Radiology provides essential diagnostic evidence Careful assessment of the saccular shadow in all views shows that it is connected with the aorta, expansile pulsation is good evidence but may be absent when thrombosis has occurred and may be confused with aortic pulsation transmitted to other tumours, linear calcification is good evidence but rarely occurs in other tumours. Angiocardiography is the most valuable method in differential diagnosis from other mediastinal swellings in difficult cases, but even with this technique clotting within the sac may mislead

The electrocardiogram in syphilitic aortitis is abnormal in some 70% of cases (*10*). The changes are due to the effects of ischæmia and ventricular hypertrophy S-T segment and T wave abnormalities are the most common Left bundle branch block is not uncommon when there is both aortic incompetence and cardiac pain Q waves from silent cardiac infarction are unusual S-T depression after effort may reveal ischæmia in a graph which is normal at rest as in the more common forms of coronary disease. An electrocardiogram which shows variation in the T wave or S-T segment on different occasions is not unusual and is evidence of coronary involvement Storey found an abnormal cardiogram in 33 of his 34 cases with cardiac pain (*10*)

Treatment of Syphilitic Aortitis

All the accepted methods of treatment for heart failure and angina pectoris are applicable when these conditions are due to syphilitic heart disease

Anti-syphilitic treatment should be used in all cases of cardiovascular syphilis There is reasonable necropsy evidence that adequate treatment with arsenic and bismuth caused healing of active luetic aortitis (*1, 11, 12*) However, penicillin has now superseded arsenic which is *potentially toxic, in the treatment of cardiovascular syphilis.* Serious reactions sometimes described in earlier reports are now rarely encountered Although there is no agreement concerning

the other hand the more protracted courses of treatment leads to default. In any case it remains to be proved that premedication

circumference was more than 8 cm. in 18 of these (4). The frequency of bacterial endocarditis in pure mitral incompetence is high compared with mitral stenosis and it affected 10 of 30 cases of pure incompetence in one selected series of hospital cases (5).

Aortic valve disease is also commonly the site of superimposed endocarditis Acquired rheumatic aortic incompetence is the usual lesion, but congenital bicuspid valves, and occasionally incompetent syphilitic aortic valves are also affected

In 89 necropsies of the Medical Research Council series the tricuspid valve was affected in four cases, but in each of these there was also mitral and aortic valve disease The pulmonary valve is rarely the site of bacterial endocarditis but after successful treatment with antibiotics exercise tolerance was improved in two cases, and it was considered that ulceration may have partially relieved the obstruction (6)

some 80% of cases Other varieties of non-hæmolytic streptococci, staphylococci and hæmophilus organisms account for most other cases but the list of indicted organisms steadily grows, and Jones (8) has presented a comprehensive list of the very many proven causative organisms

There is evidence that the proportion of cases due to enterococci (includes streptococcus fæcalis) is increasing, these organisms were responsible for ten of forty-six patients treated at the Mayo Clinic from 1950–1952 (9) In most cases enterococci affect patients with organic heart disease, however, there is evidence that normal valves may be involved (10) Brucella abortus endocarditis is probably more common than the few reports suggest In most reports the aortic valve is the site of infection (11, 12, 13); treatment is usually unsuccessful

Evidence continues to show that dental sepsis provides the most common focus of infection There were apical abscesses in 33 5% and dental extraction in 9 8% of 457 non-hæmolytic streptococcal cases (3), and 48% of the Medical Research Council series showed signs of dental sepsis or gave a history of recent extraction (1) Gastro-intestinal disease and urological procedures may be the source of enterococcal infection (10)

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BACTERIAL ENDOCARDITIS

The clinical features of bacterial endocarditis have been well known for many years, since penicillin therapy was introduced there have been no significant recent advances, but knowledge of the organisms which can cause it and the programmes of bactericidal therapy necessary to cure it have been steadily extended. Acute and ulcerating forms of bacterial endocarditis are rare now that the primary septic lesions such as osteomyelitis, carbuncle, pneumonia and septicæmia are treated effectively

Age and sex incidence. The disease is rare under fifteen years (*1*) and reaches a maximum incidence between twenty and thirty years The diagnosis is readily missed in elderly subjects who are not uncommonly affected The average age was fifty-one in a series of 33 cases of enterococcal endocarditis. There were 94 cases of bacterial endocarditis over the age of forty-five in a large series of necropsies, and four times as many men were affected as women (*2*). Male preponderance was also shown in the older age groups of the Medical Research Council series (*1*) although the overall sex incidence was about equal, below the age of thirty-five years, 59% of patients were female, and over that age 61% were male This difference is possibly related to the higher incidence of the more benign aortic valve lesions in the male There is some evidence that males are more frequently affected by the more virulent organisms (*3*)

Pathology. TYPE OF HEART LESION In the Medical Research Council series of 442 cases, the mitral valve alone was affected in 41% Although the frequency of stenosis and incompetence could not be determined it is probable that the majority of patients with mitral valve disease had dominant incompetence. necropsy confirmation of mitral valve disease alone was available in 29 and actual stenosis was reported in only 2. In 20 necropsy cases of bacterial endocarditis the mitral valve was involved in 19 and the

in conjunction with penicillin, especially in cases of enterococcal infection Enterococci are the most frequent cause of serious penicillin resistance, some cases have been cured with very high dosage penicillin alone, but a combination with dihydrostreptomycin is the most effective (10). Brucella abortus endocarditis has been cured with a combination of aureomycin, streptomycin and dihydrostreptomycin (*13*)

Bacterial endocarditis may follow cardiac surgery, twenty cases resulted from 2263 operations (*16*), a coagulase negative staphylococcus was mostly responsible Twelve died and six of these were direct failure of treatment Most organisms were very resistant to penicillin, but a response was obtained to doses of 5,000,000 to 30,000,000 units intravenously combined with intramuscular streptomycin in some cases.

Little is to be gained by listing and discussing the merits of erythromycin, oxytetracycline, chloramphenicol, chlortetracycline and the other antibiotics which have been used, because individual therapy must be ascertained by clinical trial and error together with laboratory tests

Caronamide and probenecid (Benemid) are of value with infections of high penicillin resistance These drugs temporarily block the tubular excretion of penicillin, enabling higher blood levels to be achieved There are [illegible]

[illegible] drug may have to be discontinued because of the tendency to cause severe anorexia, nausea and vomiting they are not in common use

The importance of early diagnosis and treatment is shown from a study of 118 [illegible]

trea [illegible]

[illegible] treatment in patients with highly resistant organisms [illegible]

which permittec [illegible]

PROPHYLAXIS [illegible]

should have pe [illegible]

hours before ar [illegible]

case of urologi [illegible], Gerace and Martin recommended combining penicillin with streptomycin because of the risk of enterococcal infection (*10*)

Myocardial lesions. The endocardial lesions (verruceous and ulcerative valvulitis) are well known, but the frequent and severe myocardial damage is less so. Saphir, Katz and Gore (*14*) studied the myocardial histology in 76 fatal cases and found combinations of myocarditis, perivascular infiltration, fibrosis, Aschoff bodies, infarcts and intravascular emboli, QRS-T changes in the electrocardiogram showed considerable positive correlation with the extent of myocardial damage.

Renal lesions are common in bacterial endocarditis. Minute subcapsular hæmorrhages are responsible for the "flea-bitten kidney" associated with a focal glomerular nephritis, diffuse glomerulonephritis is as common as the focal form and mixed types occur. In 100 necropsy cases 9 showed embolic glomerulo-nephritis, and in 10 others there was an acute or subacute diffuse lesion (*15*): of these 23 cases, 14 had evidence of renal insufficiency with uræmia

Clinical features. In 168 patients (*1*) the mode of onset was as follows fever and sweating (63%), cardiac symptoms (30%), peripheral embolism (20%), pulmonary embolism (10%), arthralgia (17%), gastro-intestinal symptoms (6%) and headache (5%). Early diagnosis is imperative for successful treatment, and in many cases the diagnosis should be made before the well-known signs such as finger clubbing, petechiæ, Osler's nodes and splenomegaly are present. Early diagnosis is a function of the sensitivity of the physician to relatively minor or vague symptoms in a patient who is at risk because of a particular kind of organic heart disease.

Essential investigations are hæmoglobin estimation, erythrocyte sedimentation rate, leucocyte counts and blood culture

Treatment. Penicillin remains the antibiotic of choice for most types of infection. It should be started with the first positive blood culture or on strong clinical evidence without positive culture The minimum dose is 2,000,000 units daily for five weeks Many patients require more and the dose should be doubled every forty-eight hours or so until fever is controlled It is probably more satisfactory to try doses of 8–12 mega units a day before adding or replacing with other antibiotic drugs, at this point of treatment in a resistant case, bacteriological tests should have been completed, and an appropriate drug or combination of drugs may be chosen from among the many available However, the clinical response of the patient must determine the process of trial as sometimes there are considerable differences from the response predicted by *in vitro* testing. Individualised therapy is indicated in all cases.

Streptomycin is probably the next most useful drug when used

from the United States (*1, 2, 3, 4, 5*) Adults of either sex are affected but males preponderate (*5*). The symptoms may resemble those of cardiac infarction from which it must be distinguished because of the great difference in prognosis and future management. Precordial pain occurs in over 90% (*3*), it is often intensified by respiration and usually starts abruptly, it may radiate centrifugally as does the pain of coronary disease. The most common additional symptoms are those of malaise, fever, cough, dyspnœa and vomiting. Pericardial friction is the important sign, it occurs soon after the

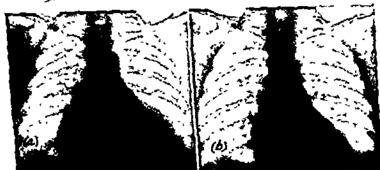


FIG 41 Acute benign pericarditis with large effusion (*a*) and resorption two months later (*b*). This patient has remained normal for 5 years.

onset of pain and usually lasts from seven to fourteen days, but may persist for many weeks Fever and leucocytosis are common in the early stage (*2*)

Radiology shows enlargement of the cardiac shadow in some 50% of cases, although this is probably due to pericardial effusion, cardiac dilatation cannot always be excluded without more elaborate methods (Fig 41)

The electrocardiogram shows changes depending on the phase of activity and the presence or otherwise of effusion At first the electrocardiogram may be normal S-T segment elevation is usual in anterior and posterior chest leads in early phases, T wave inversion may be apparent when the S-T interval becomes isoelectric Subsequently the electrocardiogram becomes normal in the vast majority

Recurrence is common and sometimes occurs several times in the months following the initial attack One patient had 19 separate attacks and showed no residual damage (*7*) The prognosis is

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3. Anderson, D. G., Keefer, C. S. 1948. *Therapeutic Value of Penicillin.* Edwards, Ann Arbor, Mich.
4. Sprague, H B. 1930. *J. Amer. med. Ass.* 94, 1037.
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9. Geraci, J E. 1952. *Minnesota Med* 35, 861.
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11. Hart, F. D. *et al.* 1951. *Brit. med J.* 1, 1048.
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15. Villarreal, H., Sokoloff, L 1950 *Amer. J med Sci.* 220, 655.
16. Denlow, C. *et al* 1957. *Circulation*, 15, 525.
17. Baker, G. P., Pilkington, T. 1952. *Lancet*, 2, 17.
18. Friedberg, C. K. 1950. *J. Amer. med Ass.* 144, 527.

PERICARDITIS

Inflammation of the pericardial sac may be acute or chronic and associated with slight exudation or massive effusion It may result from trauma, almost any infecting organism from virus to metazoal parasite (see p 156), all types of collagen disease (see rheumatic fever, p. 95 and collagen disease, p 158), blood diseases, cardiac infarction, metabolic disorders, infiltrating tumours and unknown agents The symptoms and signs are largely independent of the cause. Pain and pericardial friction are associated with acute exudation, and tamponade with more extensive effusion.

During the recent past there have been advances in the recognition of causative organisms, more frequent recognition of idiopathic or benign pericarditis, the development of treatment for early tuberculous pericarditis, improved techniques in the recognition of pericardial effusion and a clearer understanding of the hæmodynamic disorder of tamponade and pericardial constriction (see p 140).

Benign, Idiopathic, Primary or Acute Non-specific Pericarditis

The titles of this not uncommon condition indicates our ignorance of its ætiology, but it is probable that virus infection is responsible, as upper and lower respiratory tract infection is a common antecedent. It has been reported with increasing frequency, especially

disease with the development of pericardial effusion. In some cases the first features of disability are associated with pericardial constriction without effusion In the great majority of cases the disease steadily progresses with increasing disability from unresolved effusion or the development of constrictive pericarditis Occasionally, however, the disease is not only insidious in its onset, transient in its course, but ends in complete resolution (3) The initial symptoms may range as far apart as those of upper respiratory infection, rheumatism or gastro-intestinal disorder

The electrocardiogram shows varying degrees of non-specific abnormality associated with pericarditis Radiology shows an enlarged cardiac shadow when there is effusion

Differential diagnosis is essentially from other forms of pericarditis and the ætiology is confirmed by demonstration of the tubercle bacillus in pericardial fluid or on presumptive evidence of tuber-

... however, death may ensue in the early stage of the disease if serious tamponade is not relieved by aspiration Prior to the use of anti tuberculous therapy, the mortality rate in the first year after the onset of symptoms was 50% in primary tuberculous pericarditis (4) With early treatment mortality should now be less than 10% in the same period ...
grammes daily should be
INAH In early cases, w
sedimentation rate, we ha ... complete resolution of all symptoms and signs and laboratory evidence of activity as early as six weeks Many reports have now conclusively shown the great value of streptomycin treatment in early cases After aspiration of the sac, reaccumulation of effusion may be a problem Streptomycin 1 gm dissolved in 2 cc of water injected into the pericardium at each aspiration may aid rapid recovery (5)

PROGNOSIS A good ...
ment It is worse
when there is card

1 Bellet, S , Holm, S J 1957 *Circulation*, 16, 859.
2 Falk, A , Ebert, R N 1951 *J Amer med Ass* 145, 310
3 Kopelman, H 1947 *Brit med J* 1, 559
4 Wood, J A 1951 *Amer Heart J* 42, 737
5 Coe, P K 1951 *Brit med J*. 1, 18

essentially good and most investigators have stressed the absence of sequelæ, but 2 cases developing pericardial constriction have been reported; neither clinical features nor histological examinations suggested a tuberculous or rheumatic ætiology (8) We can confirm this.

Treatment. Many antibiotics have been tried without appreciably *altering the usual course of the disease, but cortisone has been* associated with rapid recovery (5). Paracentesis of the pericardium may rarely be necessary for tamponade.

Differential diagnosis is from cardiac infarction. Important points in benign pericarditis are that the chest pain is aggravated by respiration, there is often a history of respiratory infection, pericardial friction is early, widespread and persistent The electrocardiogram does not show QRS changes other than slight drop of voltage, X-rays may show effusion and the disease tends to relapse although time reveals its benign nature

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2. Brown, M. G. 1951. *New Eng J. Med.* 244, 666
3 Carmichael, D. B. *et al* 1951 *Circulation*, 3, 321.
4 Parker, R C., Cooper, H. R. 1951 *J. Amer med Ass.* 147, 835
5 Scherl, N. D. 1956. *J. Mount Sinai Hosp* 23, 293
6 Davies, D H. 1952. *Brit Heart J.* 14, 309
7. Tomlin, C E *et al* 1952 *J Amer med Ass* 149, 1215
8 Krook, H 1954 *Acta med Scand* 148, 201.

Tuberculous Pericarditis

Along with other forms of tuberculosis, infection of the pericardium is becoming rare A recent comparison between a series of cases observed in the U S A between 1930 and 1937 and a second series between 1950 and 1957, showed that the incidence of all necropsies was 0 7% in the 1930 group and 0·38% of all necropsies in the *1950* group 70% were negro in the first series and 90% in the second (*1*).

All studies show a preponderance of males, middle-aged adults are mostly affected but no age group is immune Tuberculous pericarditis may be isolated (primary), or part of generalised disease, even in primary cases the infection probably spreads from the mediastinum. Effusion occurs in many cases early in the disease and the infection may be *demonstrated by smear, culture or guinea*-pig inoculation of aspirated fluid in a large proportion of cases (2). The onset is often insidious: there may be no symptoms, or symptoms ranging from a vague general malaise to those of acute pericarditis with pain and fever. Venous pressure rises early in the

to some 60% of normal (5) and the circulation time is prolonged in most cases. The left and right atrial pressures may be about the same at 15–20 mm Hg. The high venous pressure in the right heart is reflected in a raised jugular venous pressure where a characteristic pulse wave shows the sharp diastolic collapse ("y" descent)



FIG. 42. Severe calcification of the pericardial sac

when the tricuspid valves open, and a lesser dip with ventricular systole ("x" descent) (Fig. 47). The restriction of ventricular filling leads to a very rapid rise in pressure after the nadir in early diastole which is followed by a plateau prior to ventricular systole. Similar pressure pulses exist on the left side and the high pulmonary venous pressures lead to a rise in pulmonary capillary and pulmonary artery pressures in some cases. The hæmodynamic changes produced by restricted filling also develop in some cases of cardiomyopathy, particularly in endocardial fibrosis (6, 7, 8) (page 162)

Constrictive Pericarditis

Although commonly called Pick's disease, most authorities prefer the title chronic constrictive pericarditis because its morbid anatomy and some clinical features were clearly described long before Pick associated the disease with hepatic damage (*1, 2*)

The present concepts of ætiology, hæmodynamics and treatment of the disease have developed in the last thirty years. However, the fully developed syndrome of constrictive pericarditis is now relatively uncommon and will become more rare. Males are affected more frequently than females.

Ætiology and pathology. Tuberculosis is the cause of pericardial constriction in the great majority of cases, although evidence is often indirect. The evolution from acute pericarditis to chronic constriction has been observed by Pickering (*3*) We have seen the full picture of severe constriction develop in a few months but mostly the process takes much longer. Evans and Jackson (*4*) found close contact with tuberculosis in 6 of their 30 cases and there was evidence of active tuberculosis in lung, glands and a joint in 4 other cases. Tuberculosis was identified as the result of operation in 3 further cases. It is probable that a few cases have resulted from pyogenic pericarditis, hæmopericardium (due to trauma, hæmorrhagic disease or even cardiac infarction) and virus pericarditis (see p 136)

The morbid anatomy has an important bearing on surgical treatment The heart is encased to a greater or lesser extent in a thickened obliterated pericardial sac comprising various stages of organised exudate from soft pultaceous material to calcified plate (from 1 mm. to 5 mm thick) Chronic pericarditis is often densest in the atrio-ventricular sulcus and the interventricular groove When the left atrio-ventricular sulcus is encased a sort of external "mitral stenosis" results Calcification has occurred in the sac in one- to two-thirds of patients by the time symptoms have developed. The myocardium is not seriously damaged but the subjacent muscle is often the site of inflammatory changes which bind it to the visceral pericardium; however, in some patients the pericardium and epicardium remain distinct (Fig 42)

Hæmodynamics. Many physiological studies during the last decade show that the most important effect of constriction is the limitation of ventricular diastolic filling, emptying of the ventricle is probably also affected (*1, 2, 8*) Restricted filling leads to low relatively fixed cardiac output per minute. change in cardiac output depends on change in heart rate Stroke volume is reduced

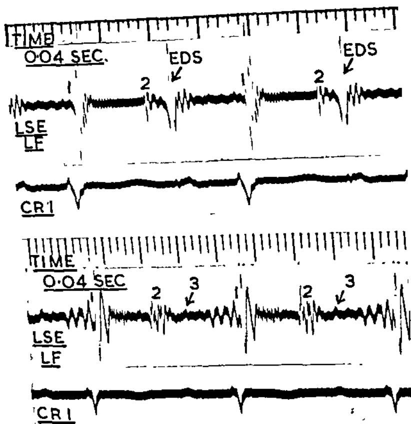


FIG. 43 Constrictive pericarditis Upper phonocardiogram shows early diastolic sounds (E D S) of comparable intensity to the first heart sound and 'louder' than the second heart sound (2) The interval between the onset of the second sound and the deflection of greatest amplitude in the E D S is 0 1 sec Lower record is from the same patient after successful operation The E D S has been replaced by a small third sound (3). The interval between (2) and (3) is 0 13 sec L S E = left sternal edge L F = low frequency

Symptoms. Dyspnœa is the most common presenting symptom (*4*, *5*). Pleural effusion, pleuritis, increased stiffness of the lung and high diaphragms from ascites may contribute to the dyspnœa The next most common complaint is of abdominal swelling and this is usually associated with less noticeable swelling at the ankles Swelling of the face, tightness of the neck and a sense of congestion when bending down are other symptoms. Unusual fatigue is quite common, as are also cough, and vague aches and pains in the chest Symptoms are often few and slight, in this disease signs are much more important.

Signs. *The signs are directly related to the abnormal hæmodynamics.* The jugular venous pressure is essentially raised and tends to rise higher on deep inspiration (Fig 55). Steep "y" descents are readily seen. Hepatomegaly, ascites and œdema are present in advanced cases Peripheral cyanosis is common and associated with a small pulse and other evidence of low output The average systolic pressure was 112 mm in one large series (*5*) The apex beat is often impalpable, heart murmurs are conspicuously absent. The first sound is usually not remarkable, the second sounds are mostly normal but the interval between them may be a little longer (varying from 0 04 to 0 1 sec.) than in healthy subjects (*4*). The most important auscultatory sign is an additional sound in early diastole which is present in the majority of patients It is usually loud and *snapping and occurs at an average time interval of 0 17 sec.* after the beginning of the second heart sound (*9*) This sound becomes softer and later in diastole after successful operation This sound appears to be associated with abrupt halting of rapid right ventricular filling, it is usually higher pitched and earlier than the third sound of ventricular failure. Its occasional absence does not exclude the diagnosis (Fig 43)

THE ELECTROCARDIOGRAM The "P" wave is abnormal in the majority of cases showing prolongation and notching (*4*) The first peak is usually lower than the second in left-sided chest leads, *indicating a tendency to left atrial preponderance* When there is atrial fibrillation the "f" waves are not remarkable The QRS voltage is usually normal, "Q" waves are never present The "T" wave is almost invariably low, flat or inverted The degree of "T" wave inversion is related to the degree of inflammation in subjacent myocardium Evans and Jackson (*4*) found that this was a means of predicting the degree of difficulty encountered in stripping the pericardium from the heart (Fig. 44).

RADIOLOGY. Cardiac pulsation is diminished in many patients,

activity The Mantoux test is usually positive. *Liver function tests* show varying degrees of abnormality. Serum bilirubin never shows more than slight elevation *Liver biopsy is rarely* indicated, in long standing cases with much hepatomegaly and ascites, the degree of congestive cirrhosis may be such that ascites will persist after a good pericardial resection (*4*); even so, operation *is not contra-indicated* by severe cirrhosis

DIFFERENTIAL DIAGNOSIS is from cardiomyopathy causing chronic heart failure Strong evidence for constrictive pericarditis is

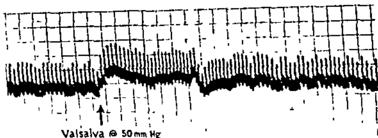


FIG 45 *Constrictive pericarditis Arterial pulse tracing shows "square wave" response to the Valsalva manoeuvre Jugular venous pressure was 15 cm above the sternal angle at 45°.*

(i) a relatively small heart, (ii) the presence of any calcification in the pericardium, (iii) steep "x" as well as "y" descents in jugular venous pressure, (iv) left atrial "P" waves exceeding right, and (v) the absence of "Q" waves (*8*)

Treatment. There are a few patients with very mild symptoms and evidence of only slight constriction who can get along without surgery and for whom *moderate medical measures suffice* (*1*), *in* all others, operation is indicated Cardiac decompression is now an established satisfactory operation resulting in relief of symptoms in some 70% of cases, however only a few entirely asymptomatic patients show entire restitution of normal dynamics Many patients have now been followed from operation for two decades Antituberculous therapy with streptomycin, INAH and PAS, should be used as a cover for operation and for a prolonged period beforehand if there is any evidence of activity Burwell has followed patients for up to 27 years after operation and almost all showed some abnormality, but most were able to work and lead nearly normal lives (*10*) The success from operation is determined by the following

the distribution of quiet areas varies according to the location of pericardial thickening. Sometimes there is excessive pulsation in other areas. A sharp outline to the heart is due to diminished movement. The cardiac shadow is somewhat larger than normal in two-thirds of patients; it is never great. Some distortion may be caused by a large liver, ascites and consequently high diaphragms A barium swallow may show left atrial distension as in mitral

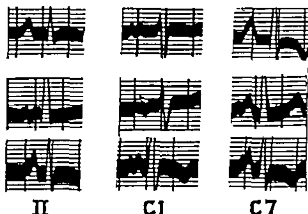


FIG 44 Electrocardiograms from three cases of constrictive pericarditis showing bifid P waves as in mitral stenosis T wave inversions in first and third cases in "left ventricular" leads

stenosis. Calcification of the pericardium is present to varying extents in many patients (Fig 42) Sometimes it encases the heart *completely. (Cœur en Cuirasse)*

The absence of calcification does not exclude the diagnosis. The superior mediastinum may appear to be widened because of a vena-caval distension and adjacent pleuritis Hilar congestion is not usually prominent, but hydrothorax and pleural thickening are common findings.

OTHER INVESTIGATIONS Cardiac catheterisation is mostly unnecessary for diagnosis, but a full study of hæmodynamics may help in assessing severity and the presence of unusual sites of constriction Neither studies of the *circulation time, nor of the circulatory responses* to the Valsalva manœuvre (Fig 45) are of special value as both *may be near normal and in fact severity may* be effectively [illegible] in most cases by clinical means and in those cases where

[illegible] nmation, but it is inconclusive; a normal sedimentation rate does not exclude

activity The Mantoux test is usually positive *Liver function tests* show varying degrees of abnormality. Serum bilirubin never shows more than slight elevation *Liver biopsy* is rarely indicated; in long standing cases with much *hepatomegaly* and ascites, the degree of congestive cirrhosis may be such that ascites will persist after a good pericardial resection (*4*), even so, operation is not contra-indicated by severe cirrhosis.

DIFFERENTIAL DIAGNOSIS is from cardiomyopathy causing chronic heart failure Strong evidence for constrictive pericarditis is

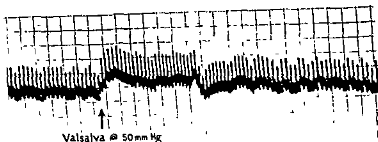


FIG 45 *Constrictive pericarditis* Arterial pulse tracing shows "square wave" response to the Valsalva manoeuvre Jugular venous pressure was 15 cm above the sternal angle at 45°.

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Treatment There are a few patients with very mild symptoms and evidence of only slight constriction who can get along without surgery and for whom moderate medical measures suffice (*1*), in all others, *operation is indicated* *Cardiac decompression is now an* established satisfactory operation resulting in relief of symptoms in some 70% of cases, however only a few entirely asymptomatic patients show entire restitution of normal dynamics Many patients have now been followed from operation for two decades Anti-tuberculous therapy with streptomycin, INAH and PAS, should be used as a cover for operation and for a prolonged period beforehand if there is any evidence of activity Burwell has followed patients for up to 27 years after operation and almost all showed some abnormality, but most were able to work and lead nearly normal lives (*10*) The success from operation is determined by the following

factors: (i) the degree to which it is possible to remove the constricting scar from the ventricles; (ii) the presence or absence of continued activity of tuberculous infection; (iii) the extent to which underlying myocardial fibrosis complicates the pericardial constriction; (iv) the presence of constrictive pleuritis; (v) the degree of congestive cirrhosis (according to Evans and Jackson this is the most important factor (*4*)); (vi) the occurrence of atrial fibrillation; (vii) unrelated burdens such as obesity, pregnancy, valve disease, renal and pulmonary disease; (viii) the development of systemic hypertension after operation (*10*)

Prevention of constrictive pericarditis by anti-tuberculous therapy early in the course of tuberculous pericarditis is now possible (see p. 139).

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2. Wood, P. 1957. *Disease of Heart and Circulation* London, Eyre and Spottiswoode.
3 Pickering, G 1948 *Quart J. Med* 17, 291
4 Evans, W , Jackson, F 1952. *Brit. Heart J* 14, 53
5. Chambliss, J. R. *et al.* 1951. *Circulation*, 4, 816
6. Helzel, P. S. *et al.* 1953. *Proc. Mayo Clin* 28, 107.
7 Clark, G M *et al* 1956 *New Eng J. Med.* 254, 349
8 Brigden, W. 1957. *Lancet*, 2, 1179
9. Mounsey, P 1955 *Brit Heart J* 17, 143
10 Burwell, C. S. 1957. *Circulation*, 15, 161.

CHAPTER 3

MYOCARDIAL DISEASE

A VARIETY of diseases which affect the myocardium are considered in this chapter The commonest causes of myocardial damage are [illegible] and inflammation from rheumatism;

affect man. Congenital, inflammatory, neoplastic, metabolic, allergic and degenerative processes may occur, and these broad groups form a satisfactory basis for classification, but there is much to be said for a division into myocarditis and myocardosis (*1*), myocarditis being associated with infections, and myocardosis with a variety of non-infectious disorders

Primary myocardial disease may cause various symptoms but those due to chronic biventricular failure are the commonest. Syncope and sudden death are features recorded by many writers (*1*, *2*, *3*, *4*, *5*, *6*) In chronic heart failure from cardiomyopathy, venous pressures are often high, the venous pulse may show a "cv" wave from tricuspid incompetence, a dominant "a" wave from right ventricular hypertension, or a Bernheim effect; sometimes a steep 'y' descent particularly contributes to the difficulty of diagnosis from constrictive pericarditis (Figs 46, 47 and 55) Murmurs are conspicuously absent although a pan-systolic murmur of functional atrio ventricular valve incompetence may be heard when there is great cardiac enlargement with failure Gallop rhythm is usually present (5)

Electrocardiograms show all the varying degrees and types of abnormality from muscle disease. X-rays likewise show a wide range of cardiac enlargement depending on the type of disease and the stage [illegible]

1 Blankenhorn, M, Gall, E A 1956 *Circulation*, 13, 217
2 Saphir, O 1942 *Amer Heart J* 24, 167

3. Karni, H. 1954. *Acta med. Scand.* 149, 244.
4. Gydell, K., Björck, G., Winbead, S. 1955. *Acta med. Scand.* 151, 1.
5. Brigden, W. 1957 *Lancet*, 2, 1179.
6. Teare, D 1958. *Brit. Heart J.* 20, 1

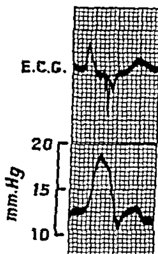


FIG 46 Left ventricular hypertrophy (cause unknown) causing "giant" "a" waves recorded in right atrial pressure curve and large right atrial P waves in E C G.

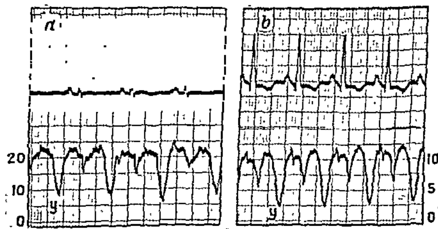


FIG. 47. Right atrial pressure curves showing high venous pressure and steep "y" descents in (*a*) cardiomyopathy and (*b*) constrictive pericarditis. Synchronous E C G above

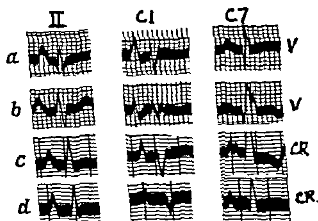


FIG. 48 Large P waves associated with chronic heart failure, and abnormalities of QRS and T waves in cardiomyopathy. (a) myocarditis, (b) familial cardiomegaly, (c) puerperal myocarditis, and (d) amyloidosis Abnormal Q waves in (a), (b) and (d)

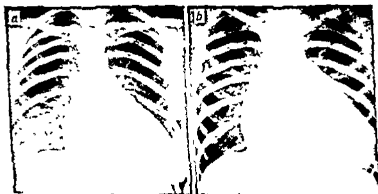


FIG 49 Cardiac enlargement with stencilled outline due to diminished movement. No pulmonary congestion (a) Puerperal myocarditis (b) Chronic myocarditis after streptococcal infection



FIG. 50 Wide range of abnormality seen on histological examination in cardiomyopathy First section shows amyloid material (A) Second is from alcoholic cardiopathy showing local necrosis (B) and mural thrombosis (C) Third section is of a case of familial cardiomegaly showing great fibrosis (D) and mural thrombus (E). Fourth section shows necrosis of fibres and cellular reaction probably due to streptococcal infection

CONGENITAL CARDIOMYOPATHY

A distinct familial heart disease was described by Evans in 1949 (*1*) Other examples of affected families have been reported since (*2*, *3*, *4*, *5*) Serious symptoms appear late Palpitation, slight giddiness, syncopal attacks, cardiac enlargement, gallop rhythm and a family history of premature death or similar disease are characteristic features. The electrocardiogram usually shows gross conduction defects (Fig 51) At necropsy, the hearts are large, having weights which are heavier than those found in other cardiopathies

Histological examination shows giant fibres with vacuolation and varying amounts of fibrous tissue, although one case (6) showed a cellular reaction as well. The pathological process presumably progresses from early life and some subjects die suddenly before symptoms develop. In others, the progress of the myocardial lesion may be observed by X-ray and the electrocardiogram, which provide evidence of continuously increasing muscle damage. The aetiology is unknown, and there may be different causes for the several types



FIG 51 Familial cardiomegaly. Sinus rhythm: ventricular extrasystoles: duration of QRS prolonged. Q waves due to fibrosis in leads I, II, and V4

of familial heart disease. There are differences between the cardiomyopathy associated with neurological conditions, the type described by Evans, and further differences were seen in a family where five of nine siblings and one of their children were affected by cardiac enlargement associated with a systolic murmur suggesting a degree of aortic stenosis; a mild degree of subaortic stenosis was found at necropsy in two of the cases (2). It may be that these diseases are hereditary and familial like Friedreich's disease and possibly inherited as a Mendelian dominant (4). When two generations are involved the maternal parent is affected in most cases (5). This may mean that the disease is more lethal in males who consequently do not reach an age to transmit the disease or that there is sex linkage, or possibly that the disease is the result of an intrauterine infection such as toxoplasmosis with special affinities for the myocardium (7). Endocardial fibroelastosis may also be familial (8, 9).

Much more information is necessary before the familial cardiomyopathies are understood. In all cases of obscure or apparently isolated myocardial disease, a full family history should be obtained,

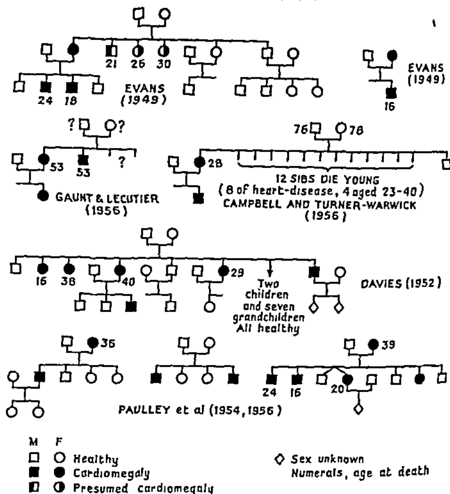


FIG 52 Pedigrees of some families reported in the literature showing more than one member affected by cardiomyopathy.

and in some cases, radiological and electrocardiographic examination of apparently normal members of the family should be made (Fig. 52)

1. Evans, W. 1949 *Brit. Heart J.* 11, 68
2. Davies, L G 1952. *Brit Heart J* 14, 206
3. Gaunt, R T., Lecutier, M A 1956 *Brit Heart J.* 18, 251.
4. Campbell, M, Turner-Warwick, M 1956 *Brit Heart J* 18, 393
5. Brigden, W. 1957. *Lancet*, 2, 1179
6. Blanshard, T. P. 1953. *Brit. Heart J.* 15, 453
7. Paulley, J. W *et al* 1956. *Brit Heart J.* 18, 55.
8. Weinberg, T., Himmelfarb, A. J 1943 *Bull Johns Hopkins Hosp* 72, 299
9 Still, W. J. S 1954. *Lancet*, 2, 1261.

MYOCARDITIS (CARDIOMYOPATHY DUE TO INFECTION)

Myocarditis is the obvious term for this group and its use should be restricted to those conditions in which there is reasonable clinical or pathological evidence that the disease is due to an infection. Most known organisms ranging from virus disease to metazoal parasites have been found to affect heart muscle, indeed more than fifty causal agents have been listed (*1*). However, it is rare for heart disease to occur as the only manifestation of such an infection and when the heart alone is affected it is unusual to identify an infecting organism, even when there has been fever, leucocytosis and raised sedimentation rate, and a histological picture of acute or subacute inflammation at necropsy

VIRUS DISEASES The influenza virus has been shown to cause myocarditis In two cases of acute non-bacterial myocarditis

...logical features are similar to those found in poliomyelitis though less frequent (*vide infra*) In the recent epidemic of Asian influenza evidence of myocarditis has been slight and extremely rare. Thirty-five cases of fatal myocarditis attributable to acute nasopharyngeal and tonsillar infections have been reported (*9*)

Myocarditis is a common feature in poliomyelitis and its prevalence probably varies in different epidemics Histological examination may show slight changes with œdema, capillary dilatation and perivascular infiltration with lymphocytes and polymorphonuclear leucocytes In more severe cases the myocardial fibres are damaged, there may be a foci of mononuclear cells and sometimes a widespread interstitial reaction Dolgopol and Cragen (*5*) found 16 cases of focal myocarditis in 92 cases dying in the acute and convalescent sta...

... there was no obvious myocarditis. The lesions are similar to those found in influenza A infection and are probably produced by the direct invasion of the poliomyelitis virus which has been recovered from human heart muscle by transfer to monkeys (*6*) Some of the myocardial changes might be due to chronic anoxia which occurs in most cases prior to death

The clinical recognition of cardiac involvement in poliomyelitis is

difficult. The signs are few and are difficult to disentangle from those produced by general illness and those due to respiratory trouble. Although both endocarditis and pericarditis are known to occur, clinical recognition is not usually possible. Arrhythmias are common; hypotension, shock and so-called peripheral failure are serious aspects and have a bad prognosis. Congestive cardiac failure may appear but it is unusual, sudden death is not uncommon

A mild elevation of blood pressure may appear during the acute stages (4) Hypertension occasionally tends to reach malignant levels and rarely hypertension may persist. Most cases of transient hypertension are caused by hypoxia, but hypothalamic lesions may be responsible in persistent hypertension Pulmonary œdema is not uncommon in severe poliomyelitis and may arise without evidence of myocardial disease; it may be due to several factors including *hypoxia, vaso-constriction, overhydration, oxygen poisoning, circulatory* changes induced by artificial respiration, and to the myocarditis itself.

The electrocardiogram in poliomyelitis shows that myocarditis is very common The whole range of non-specific abnormalities may be encountered including conduction defects and arrhythmia These abnormalities vary between 15% and 35% in different series and they appear within the first ten days and often last for several weeks.

Infectious hepatitis may be associated with myocarditis although as in the case of most other virus diseases myocardial damage is rarely of clinical significance. The many strains of *Coxsackie virus* are known to produce generalised and focal myopathy and some of the strains may produce cardiac damage Isolated myocarditis may be the only manifestation of infection with this virus (7, 8). *Ten infants from the same maternity home became ill, six died, and* necropsy was carried out in three, an acute focal interstitial myocarditis was present, and thorough virus studies showed that Coxsackie (group B) virus was responsible (7)

Rickettsial disease Myocarditis has been observed in all fatal forms 50% of fatal cases of epidemic typhus, 50% of 19 cases of Rocky Mountain Fever, and all of 227 cases of Scrub Typhus showed histological evidence of myocarditis in one large series (1), but, as in other infections, *the incidence of myocardial lesions varies in different* epidemics Vessels of various sizes are affected, and there is perivascular infiltration, nodule formation and diffuse interstitial change (9) The vascular lesions tend to cause thrombotic occlusions

and multiple small infarcts, acute circulatory failure may result (10). The QRS-T complex of the electrocardiogram shows slight to great abnormality, but return to the normal appears to be invariable with recovery from an attack of typhus fever.

BACTERIAL MYOCARDITIS This may complicate any of the known specific bacterial fevers, but it is increasingly rare. The most important effect of specific bacterial infection is by an indirect action of which rheumatic carditis (see Chapter 2) and diphtheritic myocarditis are the well known common examples. *Scarlet Fever* may cause a myocarditis (other than rheumatic) in perhaps 6% of cases (*11*). Diffuse parenchymatous and focal interstitial reactions have been observed. Whilst it is generally considered that recovery is complete, it is possible that healing may result in fibrosis which appears as a chronic cardiomyopathy many years later (*12*).

Diphtheria With the increasing use of active immunisation *diphtheritic myocarditis* is becoming uncommon. It remains, however, the most serious sequel of diphtheritic infection, and is responsible for more than half of the deaths from diphtheria (*13*). There are no very recent advances in knowledge of any aspect of this condition. Myocardial cells are primarily damaged, but an interstitial reaction occurs which may be a non-specific response to muscle death. The clinical picture varies in intensity and in severe cases the development of hypokinetic failure or severe hypotension carries a bad prognosis. The electrocardiogram shows various abnormalities. Conduction defects are especially common, and complete heart block may lead to Adams-Stokes' syndrome.

Toxoplasma myocarditis Toxoplasmosis may involve the heart in both its congenital and acquired forms. The organism has been observed in heart muscle in the acquired generalised form (*14*, *15*, *16*). The myocarditis is usually part of the generalised illness but occasionally it may be the presenting and dominant feature of the disease (*17*). In one case, proven by inoculation of heart muscle into a mouse (*18*), a diagnosis of non-specific myocarditis had been made. The patient developed progressive heart failure, and died some four months after the illness started. The dye test and complement fixation tests for toxoplasmosis were positive in life. The electrocardiogram showed left bundle branch block. The heart muscle was hypertrophied and there were foci of cells in the sections, but the toxoplasma organism was not seen (*19*).

Familial cardiomyopathy may result from toxoplasmosis (*20*, *21*), in such cases it is uncertain whether the lesions are of a chronic

acquired form or truly congenital: it has been suggested that pregnancy may reactivate toxoplasmosis in the mother, resulting in fœtal infection. If the relatives of patients with known cardiomyopathy are investigated, evidence of unsuspected heart disease may be shown by cardiomegaly on X-ray examination or a pathological electrocardiogram may be found. It is clear that in cases of subacute myocarditis, familial cardiomegaly or isolated chronic cardiomyopathy, the possibility of toxoplasmosis should be considered.

Trichiniasis. It is now well known that the heart muscle may be infected in trichiniasis. The parasite may be seen in heart muscle, but this is unusual even in cases where there has been clear evidence of myocarditis in life Trichiniasis may be mistaken for rheumatic fever because of arthralgia, fever, epistaxis and electrocardiographic abnormalities. Ventricular ectopic beats may occur and the T waves may be inverted; these signs of myocarditis may disappear with the administration of ACTH or cortisone. It has been suggested that cortisone suppresses the inflammation following the invasion of the larvæ trichinella which later become encysted *(22)*

Trypanosomiasis The myocardium is damaged in both the acute generalised and chronic forms of infection with the trypanosomum cruzei (*Chagas' disease*) *(23)* Interstitial myocarditis, and even extensive necrosis of muscle may be found in the acute form. Chagas' disease should be regarded as an essentially cardiotrophic infection by schizotrypanum cruzei The heart is affected in most cases The acute form occurs mainly in infants and children. In chronic cases, arrhythmias and conduction defects are especially common. Sometimes chronic lesions of the heart are associated with megaœsophagus. Males between twenty and fifty are more often affected than women.

1. Gore, I , Saphir, O 1947. *Amer Heart J* 34, 827
2. Finland, M. *et al* 1945 *Amer J. med Sci* 209, 455
3. Borden, C W 1950 *Amer Heart J* 39, 131.
4. Weinstein, L. 1957. *Circulation*, 15, 735.
5. Dolgopol, V B., Cragen, M D 1948 *Arch Path* 46, 202
6. Inngeblut, C. W 1950 *J Pediat.* 37, 109.
7. Javett, S N *et al* 1956 *J. Pediat* 48, 1
8. van Creveld, S., de Jager, H 1956 *Ann Pediat* 187, 100
9. Hertzog E., Rodriguez, H 1936 *Beitr z path Anat u z allg Path.* 96, 431.
10. Silva, A. G. *et al.* 1935 *Arch. Mal Cœur*, 28, 265
11. Rosenbaum, H. A. 1920 *Arch int. Med.* 26, 424

12 Brigden, W. 1957 *Lancet*, 2, 1179
13 Wesselhoeft, C 1940 *New Eng J. Med.* 223, 57.
14 Pinkerton, H , Wenman, D 1940 *Arch Path* 30, 374.
15 Nery Guimarães, F. 1943 *Mem Inst. Oswaldo Cruz* 38, 374.
16 Prior, J A. et al 1953 *Arch int Med* 92, 314
17 Bengtsön, E 1950 *Cardiologia*, 17, 289
18 Cathie, I A B 1955 *Lancet*, 1, 149
19 Potts, R E , Alun Williams, A 1956 *Lancet*, 1, 483.
20 Paulley, J W *et al* 1954 *Lancet*, 2, 624.
21 Paulley, J. W *et al.* 1956 *Brit Heart J* 18, 55
22 Segar, L F *et al* 1955 *New Eng J. Med* 252, 397.
23 Laranja, F S *et al* 1956 *Circulation*, 14, 1035

Puerperal Myocarditis

Heart failure arising towards the end of pregnancy or in the ... one of the usual causes of heart ... isease unrelated to toxæmia ... and in some patients recurrence in a second pregnancy, suggests that the relationship to pregnancy is not a coincidence The condition is not widely recognised although there have been several descriptions of the disorder since 1937, when cases with clinical findings confirmed at autopsy were recorded (*1*, *2*) recently there has been renewed interest (*3*, *4*, *5*, *6*) In one series (6) of 15 clinical cases 13 were negroes Necropsy showed patchy damage to the muscle with foci of muscle necrosis, ... heart failure was mainly

recovered from the attack Twin births are common at delivery from the pregnancy concerned The ætiology of these cases is quite obscure An analysis of 18 cases of heart failure occurring in the puerperium (7) suggested that one or more of several causes may be active, some were associated with toxæmia, ... The difficulty of differential ... s, ... ts

1 Hull, E , Hafkesbring, E 1937 *New Orleans M & S J* 89, 550
2 Goulley, B A *et al* 1937 *Amer J med Sci* 194, 185
3 Melvin, J P 1947 *Ann int Med* 27, 596.
4 Woolford, R M 1952 *Ohio M J* 48, 924
5 Bashour, F , Winchell, P 1954 *Ann int Med* 40, 803
6 Meadows, W R 1957 *Circulation*, 15, 903
7 Benchimol, A *et al* 1957 Awaiting publication in *Brit Heart J*



FIG 53. Puerperal myocarditis showing decrease in heart size with recovery from heart failure although E C G signs (V6 only is shown) show persistent S-T changes suggesting chronic myocardial injury (a) One month after delivery of a normal child. (b) 4 months later. (c) One year later (d) After 3 years

CARDIOMYOPATHY DUE TO COLLAGEN DISEASE

The heart is affected in a varying degree in all of the so-called collagen diseases, but in many cases cardiac damage is only an insignificant facet of generalised damage to organs Hypersensitivity myocarditis and serum sickness, polyarteritis nodosa, systemic lupus erythematosus, rheumatoid arthritis, scleroderma and dermatomyositis are included in this section, but rheumatic fever which is the most important collagen disorder from the heart point of view is considered separately (Chapter 2).

Hypersensitivity myocarditis and allied conditions. These are rare conditions and little is known about them. The existence of acute or subacu-
to drugs and other
carditis is mostly o
sitivity which affec
angiitis) The lesions tend to be homogeneous, located within the viscera and interstitium, and show an exudative type of reaction (*1*, *2*) In contrast, the lesions of polyarteritis nodosa affect the larger vessels and are heterogeneous, showing various stages of development

Heavy metals sulphonamides and many other drugs
the h
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branch block, but recovery may be complete (3) There was no increase in the number of cases listed as interstitial myocarditis after the introduction of sulphonamide at the Mayo Clinic (*4*)

Closely related to hypersensitivity myocarditis, in which there is a known antigen, are many cases where there is clinical or pathological evidence of allergy but no obvious ætiology Such cases mostly present a more chronic clinical picture and are rarely reversible Cases have been described with a high circulating eosinophil count (5) and having

system

Pol ... frequently damaged in primary periarteritis In a review of 175 cases (*9*) there were cardiac symptoms in 55%, hypertension in 54% and electrocardiographic changes in 64% The medium-sized branches of the coronary arteries tend to be affected rather than the smallest branches, as in hypersensitivity angiitis Inflammation of media and adventitia may lead to thrombosis in the lumen and cause cardiac infarction. Aneurysms may arise, and even rupture, causing hæmopericardium (*10*)

Hypertension is a common development in periarteritis nodosa, the reported incidence ranges from 55 to 100% and together with

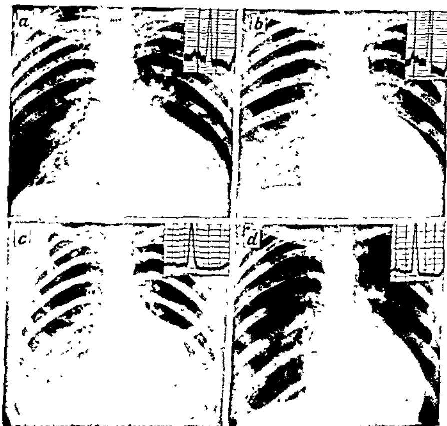


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Myocarditis is a common finding on histological examination of necropsy material but it is rarely recognised in life, and its effects are difficult to differentiate from those caused by hypertension, pericardial effusion and endocarditis. Myocarditis is one of the many causes which lead to death from heart failure. The myocardial fibres themselves are not often damaged but hæmotoxylin bodies appear to be formed from degenerating muscle nuclei. Myocardial damage is mainly interstitial where sparse granulomata, a fibrinoid lattice and occasionally patches of fibrosis may be seen.

Scleroderma. This is a disease of the mesenchyma of unknown cause, and like systemic lupus erythematosus the name implies skin disease, but as in lupus, there are also systemic lesions. Cutaneous thickenings with loss of elasticity, Raynaud's phenomenon, local [illegible]

were first described by Weiss *et al* (18) in two necropsies, and symptoms were present in all of nine cases. Various lesions may be present ranging from a vascular fibrosis to apparently acute patches of myocarditis and including perivasculitis. The atrio-ventricular valves *may* show small nodes (*19*). Macroscopically the myocardium is brown, stringy and flabby (*20*). Two main types of lesion are present [illegible]

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hear[illegible] develops. The formation of œdema under the rigid skin causes great discomfort.

The electrocardiogram may be normal but more commonly there are abnormalities such as slight prolongation of the Q-T interval, intraventricular delay, low voltage and T wave changes. Arrhythmias are not uncommon and heart block may develop.

Cortisone usually gives some improvement, but should be given cautiously, even when there is heart failure. Leinwand (*19*) reported one patient who had received treatment with cortisone for four years up to 1954.

1 Zeek, P M 1953 *New Eng J Med* 248, 764
2 Knowles, H C *et al* 1953 *Arch int Med* 92, 789
3 Lilienfeld A *et al* 1950 *Circulation*, 1, 1060
4 Fawcett, R M 1948 *Arch Path* 45, 25–35
5 Loeffler, N 1936 *Schweiz med Wschr* 66, 817
6 Lennox, B. 1948 *J Path Bact.* 60, 621–628.
7 Weiner, M J, Knight, E M 1957 *Amer. Heart J* 53, 157
8 Roussak, N J 1954 *Brit Heart J*. 16, 218

myocardial disease it is usually responsible for heart failure which is the commonest cause of death (*11*)

Systemic lupus erythematosus. This disease is not uncommon and is now well recognised. Originally it was considered to be a skin disease, but visceral manifestations have been known for a long time and Osler observed cardiac complications over fifty years ago In 1924 four cases of verrucose endocarditis were described (*12*) and damage to the heart was thought to be rare, however, more recent investigations show that from 60-90% of patients with systemic lupus have cardiac abnormalities at some stage (*13, 14, 15, 16*).

The clinical diagnosis of systemic lupus erythematosus is based on a typical skin rash, arthralgia, serositis, fever, retinal changes, albuminuria, and confirmed by a high sedimentation rate and the finding of L.E. cells in the blood

Pericarditis is common, and is probably present in all cases at some stage of the disease (*15*); it was not present in 4 of 22 necropsies but these 4 had died after an unusually short illness Some patients have recurrent brief episodes of pericarditis, whilst in others it appears to be a process of continuing activity. Pericardial friction is more common than pain in the chest. Tamponade from pericardial effusion is rarely seen, but many patients show radiological evidence of an effusion followed by resorption after a phase of activity The electrocardiogram shows T wave flattening or inversion, sometimes there is S-T elevation and often a low voltage tracing when there is a large effusion. Serial electrocardiograms are of value in following the course of the pericarditis. Constrictive pericarditis has not been observed

Endocarditis A non-bacterial, non-rheumatic valvular endocarditis of a verrucous nature was first noted by Libman and Sachs (*12*). Recognition of this endocarditis in life is often difficult. Endocardial lesions were present in 8 out of 18 cases at necropsy (*16*) but only one had had a diastolic murmur and this was of doubtful significance In a more recent series endocarditis was recognised in life in 5 of 30 patients (*15*). Small vegetations at the junction of the mitral valve leaflets and ventricular wall are the most common finding Significant stenosis of the valve has not been observed, but the development of mid-diastolic murmurs is not uncommon Aortic valvulitis may produce slight incompetence and tricuspid valvulitis has been reported (*17, 15*) Bacterial endocarditis may complicate systemic lupus erythematosus as in other conditions with abnormality of the valves.

3 Davies, J N P., Ball, J D. 1955 *Brit. Heart J.* 17, 337.
4 O Brien, W 1954. *Brit med J* 2, 899
5 Nwokolo, G 1955. *West African med J* 4, 103.

NUTRITIONAL CARDIOMYOPATHY

The Oriental form of beri-beri is rarely seen in Great Britain. Aalsmear and Wenckebach (*1*) described the rapid circulation associated with beri-beri but Keefer (*2*) found this hyperkinetic state in only one-third of the cases seen in China. Occidental beri-beri differs from the Oriental form, and often presents with signs of left ventricular disease (*3*) It is probable that chronic hypokinetic heart failure is the most common form of presentation of nutritional cardiopathy, it is always a late development. The myocardium shows hydropic degeneration and patchy necrosis with variable *fibrosis* Similar lesions have been described in thiamine deficient animals (*4*, *5*) and the lesions closely resemble those found in potassium deficiency (*6*)

Alcoholism is the important cause of nutritional heart disease in the Occident, but the existence of heart disease due to alcohol, and not to beri-beri, is still not widely accepted A series of 22 cases (*7*) shows the wide range of heart disease associated with alcoholism, but only a few cases develop high output heart failure and have a good response to thiamine (*8*) There are intermediate states but the majority of patients appear with hypokinetic heart failure and give no response to vitamin therapy in these the muscle shows mainly hypertrophy, small areas of necrosis and patchy fibrosis None of 12 patients with alcoholic heart disease in another series showed significant response to thiamine (*9*) It is perhaps significant that alcohol is frequently mentioned amongst the case histories of reports on so-called idiopathic cardiac hypertrophy in ten adult cases alcohol was a possible cause factor in four (*10*).

In a series of 50 cases of cardiomyopathy alcoholism was present in 13 (*11*) The ages ranged from 41 to 69; and with one exception all were males A few were beer drinkers who consumed vast quantities over many years, the others drank one or more bottles of spirits a day over periods ranging from 10 to 20 years Symptoms and signs appeared earlier and were more severe in the spirit drinkers All presented with dyspnœa on exertion and in several this was accompanied by palpitation None had symptoms or signs of other forms of heart disease but bronchitis was common (probably too much smoking went with the excess drinking!) Gout had occurred in

9. Nuzum, J. W., Nuzum, J. W. 1954. *Arch. int. Med.* 94, 942
10. Loque, R. B., Mullins, F. 1946. *Ann. int. Med.* 24, 11.
11. Griffith, G. C, Vural, I. 1951. *Circulation*, 3, 481.
12. Libman, E., Sacks, B. 1924. *Arch int. Med.* 33, 207.
13. Humphreys, E. M 1948. *Ann. int. Med.* 28, 12–14.
14. McGehee, Harvey A. 1954. *Medicine*, 33, 291.
15 Brigden, W. W. *et al* 1956. *Brit. Heart J.* 18, 286.
16. Griffith, G. C., Vural, I. 1951. *Circulation*, 3, 492.
17. Gibson, R., Wood, P. 1955 *Brit. Heart J.* 17, 552.
18. Weiss, S *et al.* 1943. *Arch int. Med.* 71, 749.
19. Leinwand, I *et al.* 1954 *Ann. int Med* 41, 1003.
20. East, T., Oram, S. 1947. *Brit Heart J* 9, 167–174

Endomyocardial Fibrosis (Endocardial Fibrosis)

This term refers to the morbid anatomical appearance of the endocardium in a variety of conditions of uncertain ætiology, and does not appear to represent a single disease process with the exception described below. A minor degree of endocardial fibrosis is common in any chronic form of myocardial disease, and this should not be confused with the great endocardial thickening found in an apparently specific disease occurring in Africa. Neither should this be confused with the endocardial fibroelastosis of infants which appears to be of congenital origin (see p 86).

During the past few years several reports have indicated that a disease with variable amounts of endocardial fibrosis leading to death from heart failure is common in certain parts of Africa (*1*, *2*, *3*). O'Brien (*4*) described 25 cases from the Sudan, and Nwokolo (*5*) has found the condition in Nigeria. The cause is unknown but these African cases probably have a common ætiology. Davis and Ball (*3*) find that there is extensive fibrosis of the left ventricular endocardium and adjacent myocardium, mural thrombi are common and there may be patchy calcification Fibrosis spreads up to thicken the chordæ and the posterior cusp of the mitral valve which may become incompetent Right-sided lesions are less extensive, but partial obliteration of the tricuspid inflow tract may occur. Histologically the fibrous material is largely acellular and strands of it penetrate the myocardium degenerative changes are present in myocardial fibres away from the affected area.

The clinical picture depends on the site and extent of the fibrosis. Quiet pan-cardiac failure is usual and there may be signs of organic mitral or tricuspid incompetence. Bacterial endocarditis is not uncommon.

1. Bedford, D. E, Konstam, G L. S. 1946. *Brit. Heart J.* 8, 246
2. Ball, J. D. *et al.* 1954 *Lancet*, 1, 1049.

vaso-dilator substances. On auscultation gallop rhythm from muscle failure is usual and significant systolic murmurs are uncommon. The nervous system is mostly normal, but ankle jerks may be absent

Electrocardiograms show auricular fibrillation, but when there is sinus rhythm the P waves tend to show slight right atrial preponderance The QRS-T complexes show various degrees of ventricular damage. The T waves are frequently small and inverted in the left chest leads (Fig 54), pathological Q waves do not occur, but left bundle branch block sometimes develops X-ray examination shows slight to gross enlargement of the heart (Fig. 54)

A moderately good response to routine treatment for heart [illegible]

[illegible]

damage and patchy necrosis result from feeding potassium deficient diets in some animals (6) Similar changes have been reported in man, McAllen (12) has correlated the clinical, biochemical and post-mortem findings in two well-established cases of potassium deficiency The coronary arteries may be patent but extensive muscle fibrosis is present and the muscle has a low potassium content Sternal pain indistinguishable from the pain of coronary disease may be present Electrocardiograms, as might be expected, show varying degrees of abnormality suggesting infarction with increased abnormality at periods of hypokalæmia A low potassium level should be corrected quickly and completely, if permanent myocardial injury is to be avoided

1 Aalsmear, W C, Wenckebach, K F 1929 *Wien Arch inn Med* 16, 193
2 Keefer, C S 1930 *Arch int Med* 45, 1
3 Weiss, S, Wilkins, R W 1936 *Trans Ass Amer Phys* 51, 341
4 Ashburn, L L, Lowry, J V 1944 *Arch Path* 37, 27
5 Reinhart J F 1947 *Amer J Path* 23, 879
6 Follis R H *et al* 1942 *Amer J Path* 18, 29
7 Benchimol A, Schlesinger, P, 1953 *Amer Heart J*, 46, 245
8 Jones A M Bramwell, C 1939 *Brit Heart J* 1, 187
9 Blankenhorn M A *et al* 1946 *J Amer med Ass* 131, 717
10 Levy R L, von Glahn, W C 1944 *Amer Heart J* 28, 714
11 Brigden W 1957 *Lancet* 2, 1179
12 McAllen P M 1955 *Brit Heart J* 17, 5

Sarcoidosis The myocardium is often affected in systemic sarcoidosis The muscle becomes infiltrated with tubercle-like lesions showing epithelioid cells and giant cells Such masses may form nodules large enough to protrude into the endocardium and

one patient, delirium tremens in two, and stomatitis, dermatitis, *pain in the legs and attacks of* nocturnal sweating occurred in some of the others There were no signs of serious nutritional disorders, several were plethoric and two were frankly obese Evasiveness, irascibility, indifferent co-operation and lying were common. Their true alcoholic habits were often difficult to determine

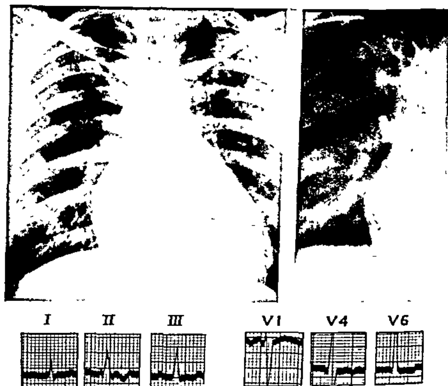


FIG. 54. Alcoholic cardiomyopathy causing moderate cardiac enlargement Right atrial catheterisation shows absence of pericardial effusion Electrocardiogram shows shallow inversion of T waves in II, III, V4 and V6

Congestive heart failure is soon apparent after the onset of symptoms, and it is of the same form found in other cardiomyopathies but with greater emphasis on left ventricular failure. Tachycardia is usual, and irregularity from extrasystoles or auricular fibrillation is common, the pulse tends to be small and examination shows no evidence of hypertension. Hyperkinetic circulation does not occur in this group and few have "hepatic" palms, increased pulse pressure or any evidence suggesting the presence of circulating

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2 Keefer, C S 1930 *Arch int Med* 45, 1
3. Weiss, S, Wilkins, R W 1936 *Trans Ass Amer Phys* 51, 341
4 Ashburn L L, Lowry, J V 1944 *Arch Path* 37, 27
5 Reinhart J F 1947 *Amer J Path* 23, 879
6 Follis R H *et al* 1942 *Amer J Path* 18, 29
7 Benchimol, A Schlesinger, P 1953 *Amer Heart J* 46, 245
8 Jones, A M, Bramwell, C 1939 *Brit Heart J* 1, 187
9 Blankenhorn, M A *et al* 1946 *J Amer med Ass* 131, 717
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12 McAllen P M 1955 *Brit Heart J* 17, 5

Sarcoidosis. The myocardium is often affected in systemic sarcoidosis The muscle becomes infiltrated with tubercle-like lesions showing epithelioid cells and giant cells Such masses may form nodules large enough to protrude into the endocardium and

heart cavity. In some cases there is relatively little involvement of other organs at the time of death. The heart is affected in approximately 20% of all cases of sarcoid.

In a review of 28 autopsy cases of myocardial sarcoid (*1*) no less than 14 of these had had Stokes-Adams' attacks or clinical evidence of *heart block*. Young adults may be affected and the condition *should clearly be suspected when there is heart block of no obvious* cause in young persons. Other arrhythmias may occur and chronic congestive heart failure sometimes results Few cases have been diagnosed in life.

1. Peacock, R A. *et al* 1957. *Circulation*, 16, 67.

Amyloidosis. Amyloid disease of the heart is often the most important, and sometimes the only, manifestation of primary amyloidosis. The heart is rarely involved in the secondary form Cardiac amyloid is not rare and there are many recent case reports in the world's literature (*1, 2, 3, 4, 5, 6*)

Amyloid, a glycoprotein of slightly varying composition, appears in the reticulum around the muscle cells, and these then disappear without a cellular reaction *It may be present in the myocardium* of any one or all the heart chambers. The pericardium is sometimes involved but the greatest amount is in the muscle; here it shows a *tendency to affect the sub-endocardial region. The atria are nearly* always affected

Cardiac failure develops insidiously. A high venous pressure with paradoxical venous pulsation is common (see Fig 55), and since the heart does not become very large, constrictive pericardial disease is particularly difficult to differentiate because hæmodynamics may be similar (7) unless there is evidence of amyloidosis *in other organs Other symptoms due to the disease elsewhere may* be slight or apparently unimportant, but hoarseness, slight dysphagia, macroglossia or an attack of purpura are important clues The *electrocardiogram distinguishes this disease from constrictive* pericarditis (*8*), in cardiac amyloid there is generally a low voltage graph *with pathological Q waves which do not occur in constrictive* pericarditis (Fig 56) No effective treatment is known Amyloid infiltration in the ground substance of the intima of the *aorta* has been described. It apparently occurs in the same distribution as atheroma (*9*).

1. Mathews, W. H. 1954. *Amer. J. med Sci* 228, 317.
2. Thomashow, A. I. *et al* 1953 *Amer Heart J.* 46 895
3. Jackson, A , Slavin, M. 1954. *Amer. Heart J* 47, 839

4 Stritch, S J , Wade, G 1953 *Lancet*, 2, 70
5 Benson, R , Smith, J. F. 1956 *Brit Heart J* 18, 529
6 Ashton, H 1956 *Brit Heart J* 18, 422.
7 Hetzel, P. S *et al* 1953. *Proc Mayo Clin* 28, 107.
8 Brigden, W 1957. *Lancet*, 2, 1179
9 MacMahon, H E , Coté, R 1957 *Circulation*, 16, 268

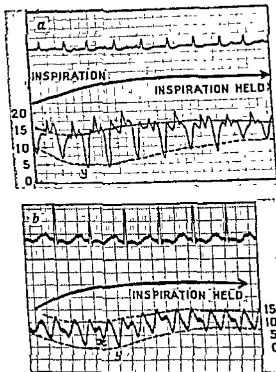


FIG 55 Right atrial pressure curves in (*a*) cardiac amyloidosis and (*b*) constrictive pericarditis There are steep "y" descents, and a rise in pressure after a transient fall on inspiration in both cases

Hæmochromatosis. Cardiac manifestations may be important and even dominant in the clinical picture of hæmochromatosis, for a fatal heart failure occurs in about 15% of cases (*1, 2*) Evidence suggests that most cases ultimately have some myocardial disease There may be some relationship between the degree of muscle activity and the amount of pigment deposition certainly there

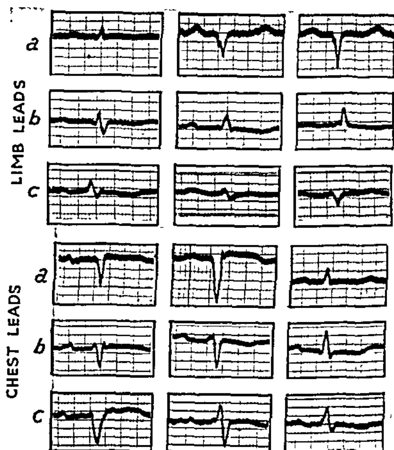


FIG 56 Electrocardiograms in three cases of primary cardiac amyloidosis The voltage is low in each There are abnormal Q waves in (a) and all show flat or inverted T waves or S-T depression in some leads. (Chest leads = V1, V4 and V7.)

is much more pigment in affected heart muscle than in muscle elsewhere In some cases the muscle fibre appears to be replaced by pigment granules and there may be 30–50 times the normal amount of iron in the myocardium Interstitial œdema and fatty degeneration may be extensive and probably play a large part in the development of failure of the muscle (3) *Fibrosis is not a* remarkable feature All chambers become diffusely enlarged

Substernal pain [illegible] disease is an interesting fe[illegible] ment and the deve[illegible] course. The development of acute right heart failure with a total

cardiac history of only 9 days has been described (4). Arrhythmias are common (5); the electrocardiogram shows a progressive lowering of voltage and T wave abnormalities common to some other diffuse cardiomyopathies

Treatment of established heart failure due to hæmochromatosis is usually ineffective but remission may follow repeated venesection (6) A similar condition of hæmosiderotic cardiomyopathy may arise as a result of repeated transfusions, in such cases venesection may bring about some improvement.

1 Sheldon, J H. 1935 *Hæmochromatosis* Oxford Univ. Press.
2 Swan, L. G, Dewar, H A. 1952 *Brit Heart J.* 14, 117
3 Levin, E B, Golum, A 1953 *Amer. Heart J.* 45, 277.
4 Bourne, G, Curston, R. J 1953 *Lancet,* 2, 917.
5 Lewis, H P 1954 *Amer. J med Sci.* 227, 544
6 McAllen, P M *et al* 1957 *Quart J Med.* 26, 231

Myotonia atrophica. Cardiac complication in this rare disease has been known for a long time. The heart is sometimes enlarged, but an analysis of 16 cases by Spillane showed that it was usually of normal size (*1*) A small pulse and low blood pressure were common A prolonged P-R interval and low voltage P waves on the electrocardiogram are features (*1, 2, 3*) The neurological signs develop earlier than cardiac ones which only appear in cases of long duration (*1*) (Fig 57)

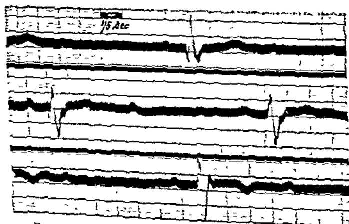


FIG. 57 Myoto [illegible]

Progressive muscle dystrophy. Heart failure from cardiomyopathy may develop in the muscular dystrophies (*4, 5*). Cardiomegaly may appear in some members of a family and myopathy in others. The weight of the heart is increased, there are degenerative changes in the sarcoplasm, and replacement of muscle by loose œdematous connective tissue Myocardial lesions have been found in sheep suffering from a form of muscular dystrophy (*6*).

Friedreich's ataxia. The heart is often affected in this disease (*7, 8, 9, 10*) The electrocardiogram was pathological in 12 of 38

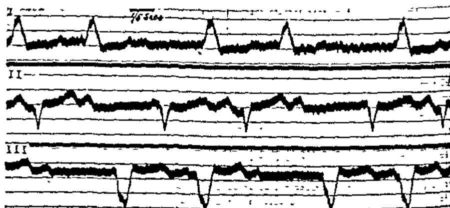


FIG. 58 Friedreich's ataxia in a twenty-two year old woman There is complete heart block and left bundle branch block and frequent extrasystoles.
(By courtesy of Dr. William Evans)

cases (*7*) although clinical examination showed abnormality in only one. These observations led Evans and Wright to state that the disease may be "as much an affection of the heart as the nervous system" The affected members of the same family tend to show identical cardiographic changes (Fig. 58)

The infrequency of clinical findings has been confirmed by other writers, but congestive heart failure is not an uncommon termination. Arrhythmias, including heart block with Stokes-Adams attacks and paroxysmal bouts of tachycardia, are common features At necropsy there may be coronary artery obstruction (*12*) but this may be incidental for some cases show interstitial fibrosis without coronary artery disease (*11*). There may be a close relationship between Friedreich's ataxia and familial cardiomegaly (*7*), as families may have some members with isolated cardiomyopathy and others with ataxia.

1 Spillane, J D 1951. *Brit. Heart J.* 13, 343.
2 Evans, W 1944 *Brit Heart J.* 6, 41
3 De Wint, L. T , Jones, J. J 1950 *J. Amer. med Ass* 144, 299.
4 Kiloh, L G , Nevin, S 1951 *Proc Roy Soc. Med.* 44, 694.
5 Storstein, O , Austarheim, K 1955 *Acta med Scand.* 150, 431.
6 Bosanquet, F D *et al* 1956 *Lancet*, 2, 737.
7 Evans, W , Wright, G 1942 *Brit Heart J* 4, 91
8 Russell, D 1946 *J Path Bact* 58, 739
9 Heijtmancik, M R *et al* 1949 *Amer Heart J.* 38, No 5, 757.
10 Manning, G W 1950 *Amer Heart J* 39, 799
11 Schilero, A. J *et al* 1952 *Amer Heart J.* 44, 805.
12 Nadas, A S *et al* 1951 *New Eng Med J* 239, 244.

TRAUMATIC MYOCARDIAL DISEASE

Non-penetrating Injuries

It is now well known that blunt injuries may damage the heart as seriously as penetrating ones Perhaps the commonest cause today is the steering wheel accident when forward momentum is arrested by collision

PATHOLOGICAL FINDINGS Necropsy after gross trauma not infrequently shows bruising of the heart muscle. The pericardium is usually affected but traumatic rupture of the heart with intact pericardium has been reported (*1*) The muscle sometimes shows hæmorrhagic [illegible]
of [illegible]
di [illegible]
de[illegible] or from 1–14 days after the injury (*3*).

Rupture of a papillary muscle in addition to contusion of the ventricular wall has been reported (*4*) and rupture of the ventricular septum may also result from non-penetrating injury (*5*) Fracture of a chorda tendina is less serious. A ventricular aneurysm may cause death months after the trauma (*6*)

It is possible that blunt injury to the heart may cause coronary occlusion (*7*), but in most cases where this is alleged to have occurred it is probable that there is existing atheroma As it is now well known that even severe coronary atheroma may be present in early adult life age cannot be used as evidence that myocardial disease has resulted from chest injury

CLINICAL FEATURES These vary greatly and partly depend on the nature of associated injuries Cardiac symptoms may be masked by shock, or the pain from skeletal injury or pleurisy. When cardiac contusion has occurred without major injury elsewhere symptoms may be absent at first Thus one man, who died later from a cardiac

aneurysm, assisted other people from the car and changed a tyre before he was seized with violent precordial pain (6). Another patient had his first attack of angina whilst walking two hours after the injury (8). Chest pain is probably the commonest symptom following blunt injury, obviously its origin in many cases is in the anterior chest wall It often is an immediate symptom but may be delayed. Symptoms from cardiac neurosis and others which may be related to the possibility of compensation are not uncommon

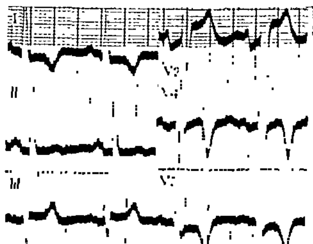


FIG 59 Angina of effort since fracture of sternum in car accident three years before Deep inversion of T waves in I, V4 and V5 due to myocardial injury

sequelæ *Pericarditis sometimes follows blunt injury. friction may* be delayed and heard up to a week or a little more after injury

Arrhythmias are not uncommon Sinus tachycardia and bradycardia, atrial fibrillation and flutter, and even heart block have been reported When atrial fibrillation develops, palpitation and dyspnœa are usual symptoms· pulmonary œdema may cause death after a severe non-penetrating injury (9)

Electrocardiographic abnormalities include the changes of rhythm already mentioned and those due to varying degrees of pericardial and myocardial injury (Fig 59)

Treatment clearly depends on the extent, site and hæmodynamic consequences of the damage Hæmopericardium seen one day after a blow on the chest required paracentesis and resulted in complete recovery in a fortnight (10) Successful suture of a ruptured heart following non-penetrating *injury has been reported* (11)



FIG 60A Hæmopericardium after a shell wound



FIG 60B The same patient with less effusion showing fragment embedded in right ventricle

Penetrating Wounds of the Heart

These are common in war but otherwise rare in the British Isles In civilian life stabbing by a knife is the usual cause. Any degree of damage may follow. Early diagnosis is essential if effective surgical repair is to be carried out. Hæmopericardium, damage to coronary arteries, perforation of the chambers of the heart, laceration of valves and chordæ have been reported from time to time.

The importance of pericardial tamponade is now recognised and it is generally agreed that relief by aspiration should be carried out as a matter of urgency (*12, 13*) Foreign bodies in the heart should be removed (*14, 15*). In future it is probable that repairs in the most complicated cases may be attained with cardiac arrest and the use of a heart pump-oxygenator (Figs 60A and B).

1. Bowman, H. S. 1953. *Amer J. clin. Path.* 23, 33
2. Barber, H. 1940. *Brit med. J.* 2, 520
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4. Glendy, R. E, White, P. D. 1936. *Amer. Heart J.* 11, 366
5 Pollock, B. E. *et al* 1952. *Amer Heart J.* 43, 273
6 O'Farrell, D. T. 1939 *Brit Heart J.* 1, 172.
7. Kissane, R. W. 1952. *Circulation*, 6, 421
8 Campbell, M 1939 *Brit. Heart J.* 1, 177.
9 Barber, H, Osborn, G R. 1941. *Brit. Heart J* 3, 127.
10 Rajasingham, A. S 1939. *Brit Heart J.* 1, 181.
11 Desforges, G. *et al.* 1955 *New Eng. J. Med* 252, 567.
12. Elkin, D. C.. Campbell, R E. 1951. *Ann Surg* 133, 623
13 Cooley, D A *et al* 1955 *Surgery*, 37, 882
14 Barret, N. R 1950 *Brit. J Surg* 37, 416
15. Harken, D E 1946 *Surg. Gynec. Obst.* 83, 117.

TUMOURS OF THE HEART

Primary cardiac tumours. These are rare at necropsy and it is exceptional for diagnosis to have been made in life Primary tumours may be benign or malignant Approximately three-quarters of those reported are benign (*1*) Myxomata are the commonest and some 75% of these are found in the left atrium (*2*) Rhabdomyoma, fibroma, lipoma and leiomyoma are the other rare benign tumours.

Malignant tumours, which comprise a variety of sarcomas, account for some 25% of the 415 case reports of primary tumours collected in 1951 (*1*). Sarcomata may arise from any part of the heart or pericardium but they are found most often in the right atrium

Secondary cardiac tumours. Malignant metastases in the heart are not uncommon In one series of necropsies in malignant disease the heart was affected in 13% (3), but in somewhat larger series the figures have been 10% of 1270 cases (4) and 10 9% of 1082 cases (5) Bronchial carcinoma is the commonest primary source and accounts for nearly one-third of the cases: this is presumably due to proximity and invasiveness of the tumour (4) Other not uncommon primary sites include breast, œsophagus and the lower gastro-intestinal tract Both sides of the heart are involved with equal frequency.

CLINICAL FEATURES The clinical picture is diverse and is due to [illegible]

atrial mxyomas may simulate mitral stenosis and pulmonary hypertension from obstruction at the mitral orifice or openings of the pulmonary veins Death may be sudden (6) or from progressive unresponsive heart failure (7) In addition to mitral systolic and diastolic murmurs one case had the loud first heart sound and an opening snap characteristic of mitral stenosis, but the correct diagnosis was made at operation by successful removal of the tumour (8)

Right atrial tumours may simulate tricuspid stenosis We have investigated one case presenting with severe polycythæmia and [illegible]

[illegible] (9) syncope related to positional change, variable paroxysmal dyspnœa, [illegible]

endocarditis In a case [illegible]

tion of the inferior ver[illegible]

and subsequently thrombosis of the inferior vena cava occurred (10)

Probably the symptoms and signs of intractable heart failure are the commonest manifestation of cardiac tumour but in many cases there are no obvious clinical features and the diagnosis is made at necropsy

In the case of *secondary cardiac tumours* the clinical picture is often dominated by the features of the primary disease When heart disease is indicated by tachycardia, arrhythmia, dyspnœa or obvious heart failure it is most likely the result of pericardial reaction to the tumour rather than the direct effect of metastatic

tumour in the heart (4). Attention of the clinician was drawn to the heart in only 20 of 127 necropsy cases of secondary tumour (4).

A full investigation is clearly necessary when primary cardiac tumour is suspect as cure by operation is possible. In the case of metastatic malignant disease elaborate investigation is unlikely to benefit the patient.

X-ray findings. Local changes of heart contour may point to a tumour but such signs are rare. A large heart shadow is most likely to be the result of pericardial effusion. Localised enlargement of chambers and the presence of pulmonary venous congestion may be due to obstruction at the valves.

Angiocardiography can show filling defects, particularly in the case of atrial tumours (11) and is the investigation of choice in such cases.

The electrocardiogram may reveal almost any type of abnormality. Many kinds of arrhythmia have been reported. Bizarre P waves may point to an atrial tumour Bundle branch block or Q waves may suggest a ventricular site. The absence of gross abnormalities does not exclude the presence of a tumour.

NON-CARDIAC TUMOURS may affect the cardiovascular system in diverse ways Carcinoid tumours of the small intestine (argentaffinoma) produce excessive quantities of serotonin (5-hydroxytryptamine) which may lead to an endocarditis affecting the right heart. Björck *et al* described the association of tricuspid incompetence, pulmonary stenosis and carcinoid (12) Several cases showing variations of the syndrome have been reported since (13, 14, 15). It appears that serotonin is "inactivated" in its passage through the pulmonary circulation (14). The diagnosis is suggested by the association of heart signs with a typical spasmodic flushing, patchy cyanosis, asthma, gastro-intestinal symptoms and particularly diarrhœa The diagnosis may be confirmed by estimating the urinary excretion of 5-hydroxy-indoleacetic acid (16) and by radiological investigation of the gastro-intestinal tract

Carcinomatosis of the lung may affect the lesser circulation by either a spreading lymphangitis or by pulmonary embolisation The clinical features of either subacute anoxia or hypertensive cor pulmonale may appear (see Chapter 5)

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3. DeLoach, J. F., Haynes, J. W. 1953 *Arch. int. Med* 91, 224.
4. Gondie, R. B. 1955. *Brit Heart J.* 17, 183.
5 Scott, R. W., Garvin, C. F. 1939 *Amer. Heart J.* 17, 431

6 Field, M H *et al* 1945 *Amer. Heart J.* 30, 230.
7 Thompson, R B. 1944. *Brit. Heart J* 6, 23.
8 Chin, E F, Ross, D. N 1957. *Brit. med J.* 1, 1447.
9 Bahnson, H. T., Newman, E. V. 1953 *Bull. Johns Hopkins Hosp.* 93, 150.
10 Cope, S 1957 *Brit med J.* 1, 987
11 Steinberg, I *et al* 1953. *Dis. Chest*, 24, 509.
12 Björck, G *et al.* 1952. *Amer. Heart J.* 44, 143
13 Thorson, A *et al* 1954 *Amer Heart J* 47, 795.
14 Goble, A J *et al* 1955 *Lancet*, 2, 1016.
15. Goble, A J *et al* 1956 *Brit. Heart J.* 18, 544
16 Sjoerdsma, A *et al* *J. Amer med. Ass.* 159, 397.

CHAPTER 4

HYPERTENSION

ALTHOUGH much work has been done in many directions the problem of the cause of hypertension is still unsolved. In fact the present tendency is to consider that hypertension arises as a disturbance of an equilibrium at several possible points (*1*); and that *it is not a disease entity in itself* (*2*).

Distinction has long been made between essential hypertension wherein the raised blood pressure is thought to be primary (hyperpiesia) and diseases in which the hypertension is secondary

The Normal Blood Pressure

TECHNIQUE. This was defined by a joint recommendation of the British Cardiac Society and the American Heart Association (*3*). It does not matter if the patient is sitting or lying The rubber bag should fit snugly over the brachial artery. It is as well to take the systolic pressure first by palpation, as difficulties over the auscultatory gap will be avoided If the cuff is then inflated well above this point, the level at which the sounds are first heard will be the systolic pressure. As the cuff is deflated the sounds become louder, then abruptly muffled (4th phase) This is the point which the British Society advised for the diastolic pressure The American Committee preferred the point at which the sounds disappeared (5th phase), and this view has been upheld more recently in that country (*4*). The point of disappearance is usually within a few millimetres of the muffling but when the pulse pressure is large, such as with aortic incompetence or hyperthyroidism, the sounds may persist to zero Direct brachial pressures recorded by electromanometer have shown that the actual systolic pressure is about 12 mm above the sphygmomanometer reading The diastolic pressure is about 3 mm. below the point of muffling but 7 mm. above the point where the sounds disappear. (*5*) It would appear, therefore, that the muffling of the sounds is a more accurate index than their disappearance If the difference between these two points is more than 10 mm , three pressures should be recorded

NORMAL VARIATIONS *Respiratory variations* may amount to 12 mm. Hg in direct recordings of the systolic pressure The Traube-

Valsalva manœuvre in which forced expiration is made against a closed glottis, the blood pressure falls during the forced expiration and rises during the succeeding deep inspiration (8)

Exercise causes a considerable, though transient, rise in the systolic pressure. In young normal subjects the systolic pressure rose up to 30 mm but fell to normal in four minutes. Most elderly normal subjects reacted similarly but in some the pressure rose by 80 mm. Mild hypertensive patients had a more pronounced rise (9)

Posture Standing up causes a fall in the systolic pressure of 10–20 mm and the diastolic rises slightly This is caused by gravity and can be prevented by standing up to the chin in water (*10*).

Effect of emotion The effect of anxiety on the blood pressure is an outstanding difficulty both in the diagnosis of an early case and in the control of the established state with hypotensive drugs. It is a truism that the patient should be relaxed and at ease, but in those with a nervous disposition the inflation of the armlet may raise the blood pressure excessively If the patient is kept recumbent for an hour or more without food and readings taken every few minutes, the "basal pressure" can be obtained, in contrast to the "casual pressure" of a single reading (*11*). These basal pressures can be surprisingly low, the systolic reading being under 100 mm in some people The same low figures may be obtained during sleep

Amytal sedation test This has been used extensively to abolish the effects of emotion Three grains of sodium amytal are given and repeated for the next two hours, unless the second dose sends the patient to sleep The pressures are taken at intervals of thirty minutes but the record when asleep is the most informative Dramatic falls of 100 mm Hg or more in the pressures may occur Unfortunately, the fact that the pressures have [illegible] normal under a se[illegible] dismissed as only [illegible] sequently have a [illegible]

Cold Pressor Test It has been suggested that those with labile pressures are more likely to develop hypertension later than those whose pressures are more stable, and the Cold Pressor Test has been used to discover hyper-reactors One hand is immersed in water at 4–6° C for a minute, and the pressure measured on the other arm Using direct arterial recordings an abnormal reaction consists of a rise in the systolic pressure of 20 mm and in the diastolic of 15 mm,

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NORMAL VARIATIONS *Respiratory variations* may amount to 12 mm. Hg in direct recordings of the systolic pressure The Traube-

the unclamped kidney is also removed (*19*). This is because the arterioles in that kidney have suffered damage on account of the hypertension from which the vessels in the clamped kidney have been protected The lesions in the unclamped kidney resemble those of malignant hypertension and comprise focal necroses of arterioles, and healed and healing infarcts. They are due to spasm of arterioles subjected to high pressure This spasm has been observed and photographed many times on the surface of the brain (*20*) The ischæmic kidney, therefore, releases a pressor substance which produces arteriolar lesions in the other kidney which then also releases pressor substances and so perpetuates the hypertension If both kidneys ...

... case of rats who were joined together soon after birth so that they had to some extent a common circulation, bilateral nephrectomy in one of the pair did not result in a rise in pressure in the other The healthy kidneys in the intact rat were able to antagonise the extra renal pressor substance entering its circulation from the nephrectomised animal (*21*) In summary, if the circulation of rats and man can be compared, ischæmic kidneys release a pressor substance capable of producing lesions similar to malignant hypertension There is also an adrenal agent which can be neutralised by healthy kidneys but which comes into play after bilateral nephrectomy

The application of this work to man lies in the finding of ...

... an aortogram showed a constriction of the renal artery at ...
of operati...
right rena...
shell of ...
ulcer dev... hypertension shortly before his sudden death and was found to have recent thrombi involving both renal arteries (*26*)

and of these the diastolic rise is the more important (*12*). This occurs within 50 or 60 sec. after immersion. In a review after six years no normal reactors had developed hypertension while 38% of hyper-reactors had done so In essential hypertension the reaction was greater, with an average rise of 37 mm systolic and 25 mm. diastolic. This tended to become less in the more severe cases of hypertension suggesting that the arterioles were becoming permanently constricted

THE NORMAL LIMITS. Most life assurance companies nowadays regard 140/90 as the limits of a normal pressure; but this is not true at all ages The average at eighty years is 170/90 (*2*) and many old people, with systolic pressures of 200 or more, have no symptoms from them. These high systolic pressures may be due to loss of elasticity of the aorta It is suggested that the lower levels for hypertension in males should be regarded as 145/90 at sixteen years, increasing steadily to 190/110 at sixty years (*13*) The figures for women are a little lower at all ages up to sixty when the average pressures rise above those of men (*14*).

Ætiology

PRESSOR SUBSTANCES Renin is a proteolytic enzyme produced by the tubular cells of the renal cortex This acts on an α-globulin, hypertensinogen, made in the liver, to form the polypeptide angiotonin, which stimulates the smooth muscle of the arterioles. If frog renin is given to dogs, made hypertensive by renal ischæmia, the blood pressure falls as anti-renin is produced and this neutralises the dog renin (*15*) It has not proved possible to produce a similar reaction in man, nor is it likely that angiotonin is the cause of human hypertension since angiotonin increases the pulmonary arterial pressure as well as the systemic, and the pulmonary pressure is normal in essential hypertension (*16*)

RENAL ISCHÆMIA Goldblatt in 1934 (*17*) produced hypertension in dogs by clamping both the renal arteries. If one artery was clamped, the pressure rose and then fell. If the healthy kidney was then removed, the pressure rose It was, therefore, apparent that renal ischæmia could produce hypertension, but only if both kidneys were involved. Either the healthy kidney could neutralise a pressor substance being formed in the ischæmic kidney, or else a depressor-substance was produced by a healthy kidney, but was not released by an ischæmic one

This work cannot be applied to human hypertension as nephrectomy, in cases of unilateral renal disease, can on occasion restore

and in the blood volume. The active agent here is probably the sodium

SODIUM Hypertension does not occur among primitive races, and it has been found that their diet is commonly low in sodium, with an average of 1–2 g (*30*). Among a large group of patients, analysed in regard to their salt intake, 12% were found to come within the low sodium range, and none of these had hypertension. It is not suggested that sodium itself causes hypertension, but that the unknown cause may not operate where the sodium level in the diet is low The effect on hypertension of virtual abstention from salt over prolonged periods in the [illegible]

Relatives of those with hypertension showed high pressures in all age groups (32)

Sex Women tolerate hypertension better than men.

NEUROGENIC CAUSES. It is doubtful whether a neurogenic element plays any part in the causation of hypertension except on rare occasions when there [illegible]

[illegible] In a case of polyneuritis due to porphyria, paroxysms of hypertension occurred, with pressures rising to 170/130 mm, associated with difficulty in swallowing (33). Procaine block of the carotid sinus, which usually causes a rise in the blood pressure, was without effect It is suggested that the same sequence may take place in bulbar poliomyelitis or post-diphtheritic neuritis if the ninth and tenth cranial nerves are paralysed Injuries sometimes cause a rise in blood pressure (*34*), *presumably* through stimulation by the sympathetic system *Fifty* casualties were found to have sustained systolic pressures from 140–250 mm of *mercury* All the men complained of severe pain. Morphia had little effect, but the pressure fell after injections of rogitine or hexamethonium and the hypertension was abolished by pentothal or spinal anæsthesia (35)

COARCTATION OF AORTA The pressures proximal to the obstruction, as in any other vascular obstruction, are high in order to maintain an adequate flow of blood to the lower part of the body and especially to the kidneys In the femoral artery the systolic pressure is lower than the normal but the diastolic is unchanged giving a small pulse pressure After a successful *resection* the

It is suggested that the contracted kidneys of some cases of chronic pyelonephritis are due to multiple ischæmic areas caused by arterial occlusions (27) In ten cases of malignant hypertension gross narrowing of the arteries was present with some evidence of re-canalisation. This arterial obstruction was not present in chronic pyelonephritis without hypertension, and the kidneys were not so contracted.

The results of nephrectomy in these cases are not good In twelve instances a successful result was obtained in only four (28) This is not surprising if it is true that after a variable time lesions will develop in the other kidney which will perpetuate the hypertension. Further, selection of cases was made on the finding of casts and cells in the ureteric catheter specimens from one kidney only. *Aortography, used to delineate the renal vessels, will probably prove more satisfactory in the future* Pyelograms are often normal.

Adrenals. PHÆOCHROMOCYTOMA The adrenal medullary tumour causes hypertension through an excess of noradrenaline The normal daily excretion of noradrenaline in the urine of 150 mg may be increased to 3000 mg. or more Intravenous injection of 1 ml. of urine from one case into a dog caused a rise in pressure (29). Patients may suffer from paroxysms of hypertension with tachycardia, prostration, sweating, anxiety and cyanosis, or the hypertension may be sustained The basal metabolic rate is raised. Intravenous injection of 5 mg. of phentolamine neutralises temporarily the noradrenaline in the blood and causes an immediate fall in the pressures Injection of oxygen into the presacral tissues may cause the tumour to be visualised on a skiagram and show the side on which it lies, but there is considerable risk in this procedure Handling the tumour at operation may cause the pressures to rise to dangerous levels unless controlled by phentolamine After removal of the tumour a noradrenaline drip is needed to prevent a catastrophic fall.

Cushing's syndrome usually comprises hypertension as well as obesity, hirsuitism, striæ, and hyperglycæmia This disease is sometimes associated with a pituitary basophil tumour, but it is now known that the adrenals are the intermediate cause of the syndrome and adrenalectomy may lead to a complete regression of symptoms The administration of extracts from the adrenal cortex such as cortisone or desoxicorticosterone, if given in excess, and especially to patients suffering from adrenal insufficiency, may lead to hypertension associated with an increase in sodium in the blood

LEFT VENTRICULAR FAILURE The signs are those of failure from any lesion by which the left side of the heart is overloaded. Dyspnœa on exertion gradually increases in intensity and is followed by attacks of nocturnal dyspnœa Gallop rhythm may be present and alternation of the pulse. The nocturnal dyspnœa may progress to attacks of cardiac asthma or acute pulmonary œdema. The pulmonary circulation is overloaded and the pressure in it rises, congestion of the pulmonary veins can be seen on screening, and the pulmonary component of the second sound increases in loudness Later the right ventricle weakens, and jugular venous engorgement and œdema appear At this stage the arterial systolic pressure may fall owing to the inability of the ventricle to maintain the necessary output

Bernheim syndrome [1910] Occasionally the signs of venous engorgement with œdema set in early with insignificant dyspnœa, and the lungs remain clear The septum thickens when the left ventricle hypertrophies (38), and when very thick, may bulge into the cavity of the right ventricle interfering with its filling Thus, as in tricuspid disease, right auricular pressure rises and large "a" waves may appear, before left ventricular failure has occurred In these cases, although there is evidence of left-sided hypertrophy in the electrocardiogram, the heart is vertical in position, so there is no left axis deviation (39)

RETINAL CHANGES These are graded into the three groups of Wagener and Keith (40) In group 1 there is thickening of the vessel walls This is shown by

with an increase in the

narrow The

of absorption These two groups occur in benign hypertension of varying degrees of severity Group 3, hypertensive

and almost bloodless In another type papillœdema may occur alone and may suggest a cerebral tumour

SYMPTOMS consist mainly of headaches or giddiness, but these are more often due to a state of mental

Claims to relieve symptoms

pressures should return to normal; otherwise the obstruction has probably not been relieved completely.

Conclusions. Animal experiments appear to have established the following facts An ischæmic kidney releases a pressor substance which causes the pathological lesions seen in malignant hypertension, and these are due to spasm of the arterioles as a result of the high pressure. There is also an extra-renal cause, probably released from the adrenals, which causes hypertension after removal of both kidneys. The adrenal pressor substance can be neutralised by healthy kidneys.

In most cases malignant hypertension is a complication of renal disease, either of nephritis or of renal infarction or pyelonephritis (*36*). In 4% only did it supervene in benign hypertension There is no anatomical cause for benign hypertension. Renal biopsies taken from patients undergoing sympathectomy for essential hypertension show, in the majority of cases, such slight abnormalities in the media of the vessels as to make it unlikely that this could cause hypertension by arterial obstruction (*37*). It is clear that the hypertension preceded the vascular thickening The cause of this primary hypertension is unknown An excess of noradrenaline can produce hypertension It is possible that essential hypertension results from the kidneys failing to eliminate or neutralise normal pressor substances secreted by the adrenals It is also possible that pressor *substances from the central nervous system through the sympathetic may maintain an abnormally high blood pressure.*

Clinical features. A sustained hypertension has important effects upon the cardio-vascular system The left ventricle hypertrophies as the result of continued overwork Narrowing and tortuosity can be seen in the retinal vessels and a failure of vision may occur from arterial or venous occlusions. Death eventually comes in 60% of patients from cardiac failure and in 25% from a stroke.

LEFT VENTRICULAR HYPERTROPHY. In a case of established hypertension enlargement of the heart is obvious The apex is outside the mid-clavicular line, the impulse is heaving in character; there may be a systolic murmur due to mitral incompetence The ringing aortic second sound is due more to elongation of the aorta than to the *blood* pressure since *this increase in length brings the* aorta nearer to the chest wall In those cases where the apex impulse is masked by emphysema or obesity the electrocardiogram may help to show left ventricular hypertrophy, or the skiagram may *show the left* border to be unduly rounded or prolonged Enlargement backwards may be seen in the left oblique view

practicable to take the basal pressure in these circumstances, but several readings can be taken and the lowest recorded An increase in pulse rate may help here or a more forceful heart beat. A history of a stroke or sudden death in one or both parents would point to [illegible]

cardiogram and by means of X-ray examination If the issue is still doubtful, and it is important to know if normal pressures can be reached, the basal pressure should be measured (45).

Grading of established hypertension. Several methods of grading cases of established hypertension are in vogue with a view to assessing their suitability for medical or surgical treatment. The simplest is to grade according to the ophthalmoscopic appearances, stage 1, consisting of those with narrowed and thickened arteries, stage 2, of those with nipping of veins; in stage 3 there are [illegible] ol exudates [illegible] it Another [illegible] cerebral or [illegible] erse factors as angina, encephalopathy or nitrogen retention is taken into account, and patients who have them are placed in lower groups (46)

Toxæmia of pregnancy. Much work has been done, without success, to discover the cause of toxæmia of pregnancy Formerly [illegible]

[illegible] years of age at some time after the 26th week of pregnancy (47) The process always starts with a rise in blood pressure This may be trivial as judged by standards of essential hypertension A casual systolic pressure of 130 is regarded with suspicion and a rise to 140/90 [illegible]

[illegible] with [illegible] albuminuria, which may be massive, occurs with œdema of eyelids and ankles This phase [illegible]

[illegible] the uterus is the only treatment If

by means of hypotensive drugs are largely fallacious The relief should be credited more to the suggestion afforded by the intensive treatment than to the treatment itself.

Hypertensive encephalopathy or hypertensive crisis. A great variety of symptoms are noted. There may be severe headaches, intense at times, nausea and vomiting; transient blindness and paræsthesiæ about the body; motor disturbance such as aphasia and paresis, or, most dramatically, severe epileptiform convulsions. Loss of memory and coma may supervene. The onset is often very sudden, but *the changes are transient and recovery is complete* The blood pressure tends to rise before the attack and the pressure of the cerebrospinal fluid is abnormally high. The local cause is cerebral angiospasm, which is part of the general vaso-constriction Sooner or later the permanent damage of hæmorrhage or thrombosis almost invariably follows these transient disturbances, but the interval is sometimes surprisingly long.

Malignant hypertension. This may be found in a variety of conditions, including acute and chronic nephritis, pyelonephritis, polyarteritis, disseminated lupus erythematosus, essential hypertension, polycystic kidney and Cushing's syndrome *(43)* *It is* characterised by a high diastolic pressure, the average being 140 mm, and a cerebrospinal pressure of over 250 mm H_2O Necrosis occurs *mainly in the arterioles of the kidney, but also in the spleen*, pancreas, liver and brain. It is probable that these are due directly to the high diastolic pressure since it has been possible to prolong the course of the disease by hypotensive, ganglion-blocking drugs *(44)* Clinically the main distinction between malignant and benign hypertension lies in the ophthalmoscopic findings of retinal œdema with papillœdema These mostly occur when the diastolic pressure is above 140 mm *(43)* Cases seen first in the malignant phase may be hard to distinguish from chronic Bright's disease, since albuminuria and hæmaturia may occur in the early stages. In those *who have been under observation prior to its development*, it becomes clear that the whole course of the disease has altered, and rapidly changed for the worse. Before the advent of hypotensive drugs the prognosis was almost invariably bad Most patients died from uræmia or cerebral hæmorrhage within a year

Diagnosis in the early stages. This is not easy The blood pressures may have been found to be raised at a routine examination, possibly for life assurance *The level may be anything from 160/100* upwards; and it must be decided whether this is a temporary rise due to nervousness or a true essential hypertension It is not

Diagnosis in a case of hypertension. If a patient presents with hypertension, the following possibilities should be borne in mind

BENIGN HYPERTENSION. The diastolic pressure is seldom more than 140 mm Hg There is no evidence of renal disease, nor of neuro retinitis

MALIGNANT HYPERTENSION. The diastolic pressure is 140 mm. or over Neuro-retinitis with papillœdema is present. The pressure in the cerebrospinal fluid may be raised. The degree of renal defect varies greatly If secondary to glomerulonephritis there will be albuminuria, granular casts and a raised blood urea. As a result of *chronic nephritis* the urine will show in addition a low and fixed specific gravity In *toxæmia of pregnancy* albuminuria may be massive Those with *pyelonephritis* will usually have pyuria; in *polycystic kidney* the blood urea is usually raised Pyelograms may reveal a *hydronephrosis* Aortograms may show vascular obstruction or infarcts in the kidney

COARCTATION OF THE AORTA The systolic hypertension is local and confined to the upper part of the body This type is likely to be found in young people

ADRENAL DISORDERS Hypertension is a feature of the *phæochromocytoma* in which it is frequently paroxysmal There will also be the additional symptoms of palpitation, sweating and nervous exhaustion In *Cushing's syndrome* increase in weight, striæ and glycosuria may be present

NEUROLOGICAL DISEASES involving the basal ganglia such as bulbar poliomyelitis This is very rare

Treatment

In recent years a number of hypotensive drugs have been introduced. They do *not* solve the problem, but attempt to break the chain of events resulting in over-stimulation of the systemic arterioles at points away from the root cause of the increased peripheral resistance

THE METHONIUM COMPOUNDS The discovery in 1945 that tetraethyl ammonium bromide could produce a ganglion blockade of the efferent sympathetic vaso-constrictor impulses and [illegible]

[illegible] tartrate Large doses were required which lead to undesirable side effects

PENTOLINIUM (*Ansolysen*) A considerable advance was made

induction of labour is delayed, eclampsia with convulsive seizures may follow soon.

Fatal malignant hypertension may supervene soon after induction in severe pre-eclampsia (*48*). In two such cases death took place from uræmia about six weeks after induction, the blood urea levels being over 400 m.

The problem as to whether toxæmia increases the liability to the later development of essential hypertension has received much attention, and it seems clear that it does, to a mild degree. In one large series primiparæ, with an average age of 18 years, whose pressures had been normal before they developed toxæmia, were followed for ten years (*49*) During that period the majority had further pregnancies and half had a recurrence of hypertension in these pregnancies At the end of the ten years 17% had persistent hypertension as compared with the 8% found by Master (*13*) in women of similar age on routine examination.

Persistent hypertension occurred three times as often after severe toxæmia than after mild, but actually it was the duration of the toxæmia that was the important point A mild toxæmia which was allowed to continue for three weeks would be more likely to produce high blood pressure than a severe attack which was terminated after a week. *It is possible that hypertension may be precipitated by* toxæmia in women who would have developed it later in any case (*50*)

In older women essential hypertension may be present before the pregnancy commences The pressure tends to be higher than in the early stages of toxæmia (*51*) Ganglion-blocking drugs have a considerable effect on essential hypertension but very little on pre-eclampsia, and their action begins to diminish before the signs of toxæmia appear (*52*).

The cardiac output begins to rise during the tenth week of pregnancy and reaches the maximum between the twenty-sixth and twenty-ninth weeks. In essential hypertension the output is not raised above the normal for the stage of pregnancy. The oxygen consumption is raised but the arterio-venous oxygen difference is also increased In pre-eclampsia, or if pre-eclampsia supervenes in essential hypertension, the arterio-venous oxygen difference *is not* increased and so the calculated figure for the output rose above the anticipated level (*53*)

POST-PARTUM *HYPERTENSION. This is of no importance* and returns to normal within six months (*47*) There is some suggestion that pituitrin and other drugs given during the third stage may play a part (*54*).

Weakness of accommodation. Paralysis of the parasympathetic causes failure of accommodation The patient may be unable to read for an hour or more after each dose. This does not matter after the nightly dose but can be disturbing at midday. Eserine drops may help.

Dryness of the mouth This is common in some degree. A tablet of Pilocarpine nitrate (grain 1/12) taken with each dose mitigates this symptom

Pulmonary fibrosis. A curious condition of pulmonary fibrosis has been found in a few patients who had been taking hexamethonium for a long time (*60*). In two cases organised fibrinous œdema with fibrosis was found (*61*) This complication has not been described with the newer compounds.

Dissecting aneurysm during methonium therapy. Of 44 cases, mainly with malignant hypertension, treated with hexamethonium or pentolinium that came to necropsy 20% had dissecting aneurysms (62) This is an unexpected finding since dissecting aneurysm is rare in malignant hypertension It is suggested that the fluctuation in the pressures may play a part, or that possibly the hypotensive agents have a specific action on the aorta

OTHER GANGLION-BLOCKING AGENTS Search continues for a ganglion-blocking agent which is effective by mouth, and with a longer action than pentolinium

Chlorisondamine (*Ecolid*) is supplied in 50 mg. scored tablets From 25 to 200 mg are taken before breakfast with another smaller dose in the even...

Presidal can be given by injection or by mouth The average subcutaneous dose...

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lasti... than that of pentolinium Two doses daily only are required Constipation is not caused but visual disturbances may be severe and some patients prefer pentolinium The average daily dose required is about half that of pentolinium There is no cross-tolerance between these drugs and pentolinium, and when they are substituted not more than 50 mg. twice daily must be given at the outset.

Mecamylamine (*Inversine*) is a secondary amine and is well

when this drug was introduced, which has now superseded hexamethonium. By the subcutaneous route it is five times as active as *hexamethonium and the oral dose required is also much less (57).*

METHODS. *Subcutaneous injections.* Pentolinium tartrate can be given subcutaneously. It is supplied in 10 cc. bottles containing *5 mg. per cc. The drug is also available combined with ephedrine to* delay absorption in 10 cc. bottles containing 10 mg. per cc Two or three doses daily are required to maintain an effective control *The initial dose is 4 mg. and the dose is increased by 1 mg. until the* systolic pressure standing has fallen to 140 mg. Hg at the trough of the depression which occurs usually about an hour after the injection, *or until signs of intolerance appear. The dose should be just* insufficient to cause the patient to feel faint when he stands for a minute at the time of the maximal effect *(57).*

Oral. The initial dose is 20 mg, three times daily and this is increased by 20 mg at a time until the desired effect is obtained. Tolerance to the drug usually occurs during the first few weeks and the dose will need to be adjusted accordingly

Pempidine tartrate (Perolysen) is more potent by mouth than pentolinium. The initial dose is 2·5 mg. three times daily. This may be increased gradually to 10 mg four or five times daily The hypotensive effect may be increased by giving at the same time chlorothiazide 0 5 g. twice daily

SIDE-EFFECTS These are due to the blocking of the sympathetic fibres, and of the parasympathetic impulses which also pass through the ganglia

Constipation is almost invariable with large doses of hexamethonium and paralytic ileus can occur. When *hexamethonium* was used in toxæmia of pregnancy three babies died from ileus and it was thought that the drug concentrated in the liquor amnii *(58). Constipation is much less severe with pentolinium* It should be corrected, as it may lead to difficulties in the adjustment of the dose, since the drug continues to be absorbed from the bowel, and over-dosage may occur. When given subcutaneously the doses are smaller and the constipation less

Hypotensive attacks. These may occur within thirty minutes of a subcutaneous injection or from one to two hours after an oral dose. The patient may faint if he stands or be unable to sit up owing to dizziness. The attacks are not dangerous and will pass off if the patient lies with the feet raised, but they are incapacitating and unpleasant and they should be avoided *Prolonged attacks with* shock have been reported either through disregard of early signs or from constipation *(59)*

each other, and there was no significant difference between them (75) Similar results were obtained in another group in which rauwiloid was used (76) There is no doubt that the rauwolfia alkaloids can lower the blood pressure and that some patients can have their pressures controlled by them alone

The effect, when taken by mouth, takes time to develop, and may be brought about th

... of the rabbit owing to the release of noradrenaline, and the vaso-constriction does not occur if reserpine has been given previously (77) Improvement usually occurs in a fortnight (76) but may be delayed up to three months (74) When reserpine (Serpasil) was given intravenously, however, the maximal fall occurred in from 1½ to 4 hours, the
A similar effect
was felt that t
to its sedative ... No significant increase in renal plasma flow was found after reserpine (79).

Side-effects These are slight and consist in the main of nasal congestion, some looseness of the bowels, drowsiness and lethargy The only serious complication is depression and this seems to be confined to reserpine
is rare with rauwiloid,
In one series treated w
depression one patie
admitted to a mental h... The symptoms are restlessness, insomnia and a sense of panic Bradycardia is common with reserpine, but not with rescinnamine The pulse rate may fall to under 40 a minute

PENTOLINIUM WITH RAUWOLFIA The combined use of rauwolfia with pentolinium was first suggested by Smirk (80) who found that less pentolinium was required When rauwiloid 4 mg was given to patients previously stabilised with pentolinium alone, it was possible to reduce the dose of pentolinium to an average of one-third of that which was formerly required; and there was a considerable decrease in the undesirable effects of the ganglion-blocking agent (81) Moreover, some of the side-effects of rauwolfia counteract those of pentolinium, the tendency to looseness of the bowels lessens the constipation, the sedation and slowing of the heart also help It is usual now to give rauwolfia in addition to a ganglion-blocking agent..

absorbed from the gastro-intestinal tract. Consequently it is equally effective by mouth as by injection *(66)*. The drug is supplied in 10 mg. tablets scored into quarters. The action is rather more prolonged than that of pentolinium. The trough occurs in two hours and the pressures return to control levels in 6–12 hours *(67)*. Mecamylamine does not seem to act only by ganglionic blockade, as before an intravenous dose takes effect 30–60 minutes elapse which is much longer than with the pure ganglion blockers There may also be an action on the central nervous system and a direct effect upon the intestines and the heart *(68)*. The initial dose is 2·5 mg. three times daily, up to 40 mg. per dose have been given, the average being 20 mg. *(69)*. The results after 1½ years were good in 14 out of 20 patients, the diastolic pressure falling to 90 or less As with other ganglion-blocking agents, the combination of rauwolfia with mecamylamine, will often allow a satisfactory result to be obtained with smaller doses and so with less severe side-effects Side-effects are prominent and constipation, dry mouth and visual disturbances are common It is better to give the largest dose at night *(70)*

Dibenzyline (Phenoxybenzamine) lowers blood pressure but is apt to cause weakness and orthostatic tachycardia. When rauwolfia was added the average dose of dibenzyline required was reduced from 670 mg. to 70 mg daily and the patients were able to tolerate the side-effects *(71)*.

Rauwolfia serpentina. This root has been used empirically in India for a variety of conditions for 3000 years, but Vakil in 1940 *(72)* showed that the main action was hypotensive It is a sedative, and also stimulates mildly the intestinal and bronchial muscles *(71)*. The drug is active when taken by mouth and is obtainable as the crude root, or as a selection of active alkaloids *(rauwiloid)*, or as the two most active alkaloids reserpine and rescinnamine. The comparable doses of these preparations are 250 mg of the crude root, 4 mg of rauwiloid, 1 mg of reserpine, 6 mg of rescinnamine *(73)*. It was found that these doses could be considerably exceeded without leading to intolerance but that there was little increase in the hypotensive action Using double doses no appreciable difference was noted between the activity of the four preparations in a large series, about half the patients responding to each one. The less severe cases did better. In another series reserpine (Serpasil) was used in doses of 0·5–2 mg. daily and the same proportion had a good result, with a mean fall in the diastolic pressure of 47 mm. *(74)* Some reduction in pressure was reported, however, in every case in one series in which the four preparations were tested against

and collapse of the circulation. The diet is now seldom used, and only in combination with drugs such as pentolinium, or with surgery

SYMPATHECTOMY. The aim is to abolish all sympathetic stimulation from the lower part of the body. Both sympathetic trunks with the splanchnic nerves are removed from the level of the 8th thoracic to the 1st lumbar This can be done as a one-stage (45) or two-stage operation (90) In these with angina or tachycardia it is better to remove the sympathetic nerves from the inferior cervical to the 12th thoracic ganglion The advantages of

patients will respond (60) Claims that the life expectancy is longer with sympathectomy than with medical treatment (45) have not included patients treated with the most recent drugs (46) There can be little doubt that the operation is falling into disuse. It should be reserved for those who feel they cannot carry out the severe and prolonged medical régime

Conclusions. There are a number of drugs from which to choose

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Since there is no cross tolerance between these compounds a combination of
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this method about one-third of patients have eventually been able to manage with rauwolfia only

HYDRALLAZINE (Apresoline) acts on constricted smooth muscle in the walls of medium sized vessels *(82)* It is stated to dilate the renal and uterine vessels, and so has been used in the toxæmia of pregnancy. The renal blood flow is increased in many cases *(83, 84)* *Hydrallazine* can be given intravenously or intramuscularly in doses of 10–20 mg. The pressure begins to fall in about 10 minutes and the maximal effect occurs in about 30 minutes *(85)*. 30 mg. given *intravenously* caused an average fall of 40% in the diastolic pressure. It is supplied also in 25 mg. tablets for oral administration The initial dose is 25 mg. four times daily, which is increased until the desired reduction is obtained, or until the side-effects are prominent. These include headache, palpitation and rhinitis, and were severe in 30% of patients *(86)*. Angina pectoris may be caused Intravenous hydrallazine caused depression of the RS-T junction *(87)*. An average oral dose was 350 mg. daily. In about 10% of patients who have been taking substantial doses over a prolonged period, a febrile rheumatic syndrome may develop This resembles rheumatoid arthritis, with pleural and pericardial serositis. Lupus erythematosus cells have been found in the marrow. Unless the drug is stopped as soon as the patient complains of pains in the joints, the syndrome may persist for months The arthralgia can be relieved rapidly with cortisone *(88)*

Hydrallazine can be used in combination with pentolinium and rauwolfia. Toxic reactions are, however, frequent and often necessitate the withdrawal of the drug.

VERATRUM VERIDE (Veriloid). This drug has been known as a hypotensive agent for a long time but the toxic dose is so near to the effective dose as to make it of little practical value. Of the alkaloids *Neogermitrine* by mouth was found to have only 0·1 mg between the toxic and the effective dose which varied from 0·5 to 0·8 mg. *(89)* The effective dose of *Protoveratrine* was about 1 mg The maximal effect of each occurred in 1–1½ hours *Toxic symptoms which comprise vomiting, choking and hiccough became more* frequent after giving the drug for a month

RICE DIET This diet, containing virtually no sodium, if continued for months, undoubtedly causes hypertension to recede Not only do the pressures fall but retinopathy disappears and the heart becomes smaller Possibly deprivation of sodium leads to decreased activity of the adrenal glands. The diet is, however, severe and the effect does not equal that of the ganglion-blocking drugs. Prolonged deprivation of sodium may lead to the low-salt syndrome characterised by reduced renal flow, muscular cramps

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TREATMENT OF HYPERTENSIVE ENCEPHALOPATHY AND ACUTE PULMONARY ŒDEMA. Pentolinium 1 mg. should be given intramuscularly, and the injection repeated in an hour. The second dose may be 2 or 3 mg. but the initial dose should not exceed 1 mg. since in some patients the pressures may fall excessively.

TREATMENT OF MALIGNANT HYPERTENSION Fifty patients with malignant hypertension, but with a blood urea of less than 60 mg, have been treated with three injections of pentolinium daily, and with reserpine by mouth, and half are living after five years (*11*) This is a considerable advance on what has been achieved by other methods of treatment Retinopathy disappeared, hæmorrhages in a few weeks, papillœdema in a few months. The signs of heart failure might go and the heart become smaller.

TREATMENT OF BENIGN HYPERTENSION. The treatment of essential hypertension is a more difficult problem since the course of the disease is so variable Many patients continue free from symptoms for years without special therapy. If they have evidence of retinopathy or left ventricular enlargement, they should be treated in an endeavour to prevent further progress of the disease and because they may pass into the accelerated form of malignant hypertension. Since there is no urgency, oral preparations are to be preferred Rauwolfia should be given for a few weeks, and if the pressures are still high, hydrallazine can be started in doses of 25 mg four times daily We have found it best not to exceed a daily dose of 300 mg. and the patient is told to stop the drug if headaches or palpitation ensue, or if the joints become painful or swollen. Finally pentolinium is begun in doses of 20 mg. three times daily or mecamylamine, or perolysen 2 5 mg can be given twice or three times daily. The dose of pentolinium is increased by 20 mg each week, and of perolysen or mecamylamine by 2·5 mg. until the pressures have fallen to satisfactory levels or signs of intolerance appear Any constipation should be treated with laxatives but the dosage should be regulated so that the patient is not troubled with dizziness or visual disturbances. The attainment of normal pressures should not be sought at the expense of making the patient feel miserable since the cardiovascular system may be afforded considerable relief when the pressures are still above the accepted normal.

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CHAPTER 5

PULMONARY HEART DISEASE

PULMONARY heart disease is a disorder of the right heart with or without heart failure: it results from disease of the lung parenchyma, or the pulmonary vascular tree, or both. Lung disease which is secondary to heart disease is excluded. In all forms of pulmonary heart disease there is a reduction of the total pulmonary

disease

Pulmonary heart disease includes many unrelated conditions which have little in common beyond pulmonary hypertension and hypoxia some may develop as an acute condition, whilst in others the process is insidious and protracted over many years There are many variable and overlapping cardio-pulmonary factors which contribute to the clinical picture in every case, so that no definitive classification is entirely satisfactory The accepted division into acute, subacute and chronic types of cor pulmonale has little to recommend it, since neither ætiology, pathogenesis nor abnormal function is indicated Furthermore, any one causal mechanism such as pulmonary embolism may occur as either an acute or a chronic condition

At present, if classification is required at all, it would seem reasonable to divide these diseases into the two groups of hypoxic or hypertensive cor pulmonale, based on the dominant functional disorder However, any one ætiology may present as a clinical problem in either group, thus whilst emphysema or cystic disease usually belongs to the hypoxic group occasional cases present as hypertensive pulmonary vascular disease This wide range of diseases is represented at one end by hypoxic emphysema without

or idiopathic pulmonary

Chronic obstructive emphysema. (Emphysema heart disease or chronic cor pulmonale.)

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63%
ailure
p 208

(5). Other causes of chronic cor pulmon

and p 213 *et seq*

PATHOGENESIS The *clinical* features of pulmonary heart disease and its rate of development depend on the relative severity and interaction of many causes, of which *anoxæmia* from respiratory insufficiency, and *pulmonary hypertension* from reduction of the vascular bed are the most important. These two

present in chronic pulmo

Vital capacity and whilst the residual volume of the is increased to some 30% of total lung volume (6) he CO_2 tension is ive obliteration of alveolar-capillary surface by chronic inflammation, bronchiolar obstruction, actual reduction in number of alveoli and vascular shunts in areas of damaged lung tissue (7, 8, 9). Chronic arterial hypoxia causes hypervolæmia, increased cardiac output and polycythæmia (when the arterial saturation is below

obstructive pulmonary arterial disease (see p 213), rarely severe

some fixed structural changes are present because the pressure is raised in a proportion of patients at rest, and before the development of failure (*12, 10*) In the early stages pressure is only raised on exercise the first evidence of failure being an elevation of right *ventricular end diastolic* pressure to some 7–10 mm Hg on exercise (*13*)

The increased resistance responsible for pulmonary hypertension is due to a great reduction in total pulmonary vascular bed This is the result of loss of vessel-bearing lung tissue, the replacement of lung with a vascular scar tissue, perivascular inflammation and obliterative endarteritis, *medial* hypertrophy and even atheroma Furthermore, hypertension is increased by the greater viscosity of

Secondary emphysema associated with kyphoscoliosis, asthma, pneumoconiosis.

Severe chronic pulmonary fibrosis associated pneumoconiosis, bronchiectasis, tuberculosis, sarcoidosis.

Diffuse interstitial fibrosis (Hamman-Rich) and miliary carcinomatosis.

Cystic lung disease.

Massive obesity (hypoventilation syndrome).

Hypertensive pulmonary vascular disease.

Primary pulmonary hypertension.

Secondary pulmonary hypertension (excluding primary heart disease)

Pulmonary embolism—repeated and small, or single and massive (with or without pulmonary thrombosis)

Collagen disease. Pulmonary arteritis.

Schistosomiasis

Parenchymal disease usually presenting with hypoxia but occasionally with dominant hypertension, e g carcinomatosis and cystic disease.

EMPHYSEMA HEART DISEASE AND OTHER CAUSES OF ANOXIC COR PULMONALE

Much fruitful research into the problems of chronic cor pulmonale *during the past two decades has led to a clearer understanding of this disease and rationalised its treatment* In this condition right ventricular hypertrophy and eventually heart failure results from respiratory insufficiency, which is always due to chronic disease of the lung parenchyma. The clinical picture at any stage is due to an interplay of many factors in the cardio-respiratory system: outstanding features are arterial unsaturation, pulmonary hypertension and polycythæmia. The incidence of chronic cor pulmonale ranks with ischæmic heart disease, hypertension and rheumatism (*1*), but in rural areas it is much less common so that the overall incidence in the British Isles is probably between 5 and 10% of all organic heart disease (*2*) Males over 45 are the usual victims

Ætiology. The commonest cause of chronic cor pulmonale is chronic bronchial inflammation due to infection, air pollution, smoking, and changes in temperature and humidity, associated with the development of diffuse obstructive emphysema Chronic severe bronchial asthma with secondary emphysema (*3*) and kyphoscoliosis with emphysema may lead to the same type of anoxic cor pulmonale

has been shown that the arterio-venous oxygen difference is normal, irrespective of the presence or absence of failure. There is a high

not provoke a further adequate increase. When failure is severe and prolonged, and pulmonary vascular resistance is high, the cardiac output falls below normal values

A derangement in function is concerned in all of these deviations from the normal; with effective treatment anoxæmia may be diminished and followed by a fall in cardiac output, pulmonary hypertension, and in the degree of polycythæmia.

Clinical features. The clinical features of congestive heart

signs of moderate pulmonary hypertension are unreliable in the presence of emphysema

The *onset* of heart failure is recognised by the appearance of œdema and a raised jugular venous pressure Even at this stage emphysema may make auscultation of little value, but in some cases an abnormally loud pulmonary second sound and even a pulmonary diastolic murmur may be heard A right ventricular gallop rhythm may be heard high in the epigastrium where a forcible pulsation of the right ventricle may be seen and felt Radiography is the only reliable method of assessing cardiac enlargement in emphysema Polycythæmia strongly suggests that the heart is involved, even in the absence of failure (*12*) Moderate finger clubbing is often

Radiological examination shows suggestive or conf

secondary branches are enlarged, but in the periphery vascular markings are diminished Late in the disease right heart enlargement becomes apparent (Figs 62A and 62B)

polycythæmic blood, and the augmented cardiac output of chron anoxæmia adds yet another factor. Although the exact mechanis is unknown it is clear that anoxæmia *per se* is responsible for son increase in pulmonary artery pressure (*14, 15, 16*). Pulmonar resistance is in the extreme range of 10 units or more in abor 20% of cases (*2*).

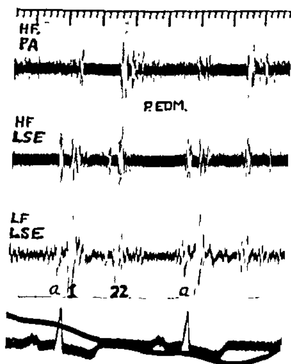


FIG. 61. Phonocardiogram shows pulmonary diastolic murmur (P.E.D M) in anoxic cor pulmonale with exceptionally high vascular resistance. *a* = large atrial sound 1 = first sound 2 = second sound H.F = high frequency L.F = low frequency P A = pulmonary area. L S E. = left sternal edge

CARDIAC OUTPUT in chronic pulmonary heart disease may be above or below normal resting values. Anoxæmia, hypervolæmia, infection and raised oxygen consumption tend to increase cardiac output, but when clinical failure is present the cardiac output is inadequate for the demands of the body. The renal blood flow and glomerular filtration rate are depressed during failure, and improved during recovery (*17*). Temporary episodes of renal ischæmia may precede the development of congestive heart failure (*17*). It

Electrocardiography. Here also difficulty is encountered in separating those signs due to emphysema alone (vertical axis and RS complexes extending across to the left chest leads), and those signs which, often appearing late in the disease, indicate definite right heart hypertrophy. Tall P waves are best seen in lead 2 derived from VR and VF and in V1 or CR1 (P. pulmonale) and these indicate right atrial hypertension The earliest signs of right ventricular hypertrophy is the appearance of a small secondary R wave in right-sided chest leads (V4R to V1) (*19*) In chronic cor pulmonale it is unusual to see extreme evidence of hypertrophy with monophasic R waves in the right chest, as seen in hypertensive pulmonary vascular disease, but in late stages of chronic emphysema heart it is common to find a rSR′ pattern in aVR and right pectoral leads: the secondary R wave is relatively tall and late Right ventricular strain may be

... pulmonary artery pressure (associated with fresh lung infection and heart failure) may be associated with negative T waves from V1 to V5. Right ventricular hypertension may occur in the ... cardiogram but definite E(trophy is not found in the (19) (Fig. ...

... infection, and in some cases continuous chemo-prophylaxis may be advisable Where financial and social factors permit, residence should be away from industrial areas Smoking should be forbidden.

Heart failure Patients in emphysema heart failure benefit from digitalis ... ev ot de (2 ... indicated where there ... and ...

... in the most severe cases



FIG. 62A. Chronic hypoxic cor pulmonale due to emphysema and asthma. At necropsy right ventricle nearly as thick as left. No occlusion of main branches of pulmonary artery Giant emphysematous *bullæ*.



FIG 62B Primary pulmonary hypertension No disease of lung parenchyma. Massive right ventricle and large main pulmonary artery at necropsy

Electrocardiography. Here also difficulty is encountered in separating those signs due to emphysema alone (vertical axis and RS complexes extending across to the left chest leads), and those signs which, often appearing late in the disease, indicate definite right heart hypertrophy. Tall P waves are best seen in lead 2 derived from VR and VF and in V1 or CR1 (P. pulmonale) and these indicate right atrial hypertension The earliest signs of right ventricular hypertrophy is the appearance of a small secondary R wave in right-sided chest leads (V4R to V1) (*19*) In chronic cor pulmonale it is unusual to see extreme evidence of hypertrophy with monophasic R waves in the right chest, as seen in hypertensive pulmonary vascular disease, but in late stages of chronic emphysema heart it is common to find a rSR pattern in aVR and right pectoral leads the secondary R wave is relatively tall and late Right ventricular strain may be detected in leads placed higher on the chest wall (V2 in 3rd I.C.S.) where a secondary R wave greater than 4 mm was frequently found in coal miners with pneumoconiosis (*20*) Acute rises in pulmonary artery pressure (associated with fresh lung infection and heart failure) may be associated with negative T waves from V1 to V5 Right ventricular hypertension may occur in the presence of a normal cardiogram but definite ECG evidence of right ventricular hypertrophy is not found in the presence of normal right heart pressures (*19*) (Figs. 63 and 64).

Treatment. Prophylaxis is important. Patients with chronic lung disease should receive vigorous antibiotic therapy for threatened lung infection, and in some cases continuous chemo-prophylaxis may be advisable Where financial and social factors permit, residence should be away from industrial areas. Smoking should be forbidden

Heart failure Patients [illegible]
digitalis, althou[illegible]
even harmful [illegible]
other f[illegible]

[illegible] polycythæmia
[illegible]rawn every few

[illegible] requires treatment and its consequent anoxæmia relieved as far as possible. Oxygen therapy is indicated in the acute stages and mostly prove[illegible]
[illegible]



FIG. 62A. Chronic hypoxic cor pulmonale due to emphysema and asthma. At necropsy right ventricle nearly as thick as left. No occlusion of main branches of pulmonary artery. Giant emphysematous bullæ.



FIG. 62B. Primary pulmonary hypertension. No disease of lung parenchyma. Massive right ventricle and large main pulmonary artery at necropsy.

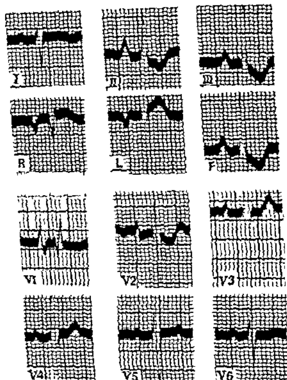


Fig 64 ... P waves ... trophy ... pulmonary vascular ... and at necropsy right and left ventricular muscle equal.

antibiotics, whether or not there is overt lung infection, broncho-dilator drugs and a sedative cough linctus In the recovery phase breathing exercises are useful, and postural drainage may be indicated The induction of ...

... is effectively treated, and alveolar ...

oxygen carries considerable risk (25), carbon dioxide retention is a late manifestation of *cor pulmonale, and at this stage hypoxia is* the only stimulus to respiration, thus oxygen administration may

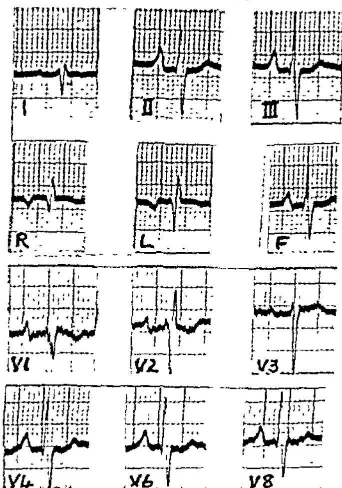


FIG. 63. Chronic hypoxic cor pulmonale due to asthma and emphysema. P "pulmonale" best seen in leads II and III. Similar patterns in VR and VL due to vertical heart and deep S waves from V3 to V8 due to rotation Only slight right ventricular hypertrophy at necropsy.

result in respiratory paralysis, acidosis and death. Although oxygen poisoning is relatively rare, and never occurs in the early stage, there is much to be said for using intermittent oxygen therapy in all cases. Control by careful clinical observation is essential, and in patients with definite CO_2 retention, gas mixtures containing less

of cases of long standing generalised pulmonary sarcoid have marked abnormalities in function, organisation of lung tissue leads to increased work of breathing, obstructive emphysema and a low diffusion capacity. Hypoxic cor pulmonale with moderate hypertension develops in relatively few cases (1, 2) Obliterative endarteritis is rarely present, but the picture of hypertensive pulmonary vascular disease does not arise as parenchymal lesions in the lung determine the clinical features

1 Stone, D J *et al.* 1953 *Amer J Med* 15, 468
2 McClement, J H *et al* 1953 *Amer. Rev.* 67, 154.

Cystic lung disease. Honeycomb Lung Disease may affect all of both lungs or only a part of one If the patient with diffuse disease survives the hazards of pneumothorax, pneumonia and renal failure (in congenital cystic disease) chronic pulmonary heart disease is a likely development (Fig 65). Respiratory insufficiency

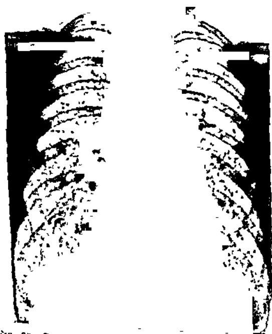


FIG 65 Cystic lung disease leading to anoxæmia, severe pulmonary hypertension and death from heart failure. Same case as Fig 66

improved, a considerable improvement in all aspects of anoxic cor pulmonale is possible. The outlook for this condition is not as gloomy as it was in the past.

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11. Hecht, H. 1956 *Circulation*, 14, 265.
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20. Thomas, A J. 1951. *Brit Heart J.* 13, 1.
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23. Mack, I., Snider, G 1956. *Circulation*, 13, 419.
24. Wilson, R. H *et al.* 1955 *Ann int Med.* 42, 629
25. Harvey, R. M. *et al* 1953 *Circulation*, 7, 932

Other causes of hypoxic pulmonary heart disease. In other types of lung disease which lead to hypoxic pulmonary heart disease the ætiology and pathology may be very different from emphysema but the physiological derangements which lead to right heart failure are similar. The degrees of anoxæmia, pulmonary hypertension and polycythæmia and their rate of development determine the

monary heart disease and it is a common terminal event in silico-tuberculosis. Asbestosis, beryllium fibrosis, scleroderma, sarcoidosis, cystic lung disease, radiation fibrosis, and long standing tuberculosis with scarring, pleural thickening and the results of extirpative surgical therapy are other less common causes.

Sarcoidosis. This condition may lead to extensive chronic fibrosis in the lungs and ultimately to cor pulmonale The majority

cause is unknown. The walls of alveoli are thickened and the interstitial tissue of the lungs undergoes a progressive diffuse fibrosis: this leads to difficulty in diffusion and greatly increases the work of breathing. At first it was considered to be an acute condition (1) but many cases have been described in which the disease runs a fatal course after many months or even after several years.

The symptoms are mainly respiratory. Dyspnœa may be severe even at rest. Anoxæmia is marked and clubbing of the fingers appears. There may be no signs at an early stage, but later fine adventitious sounds may be heard over both lungs. Although in some cases death may occur from acute respiratory failure (2), sooner or later hypoxic cor pulmonale develops in others (2, 3, 4). Severe pulmonary hypertension may occur (5) but is unusual in this rather rare disease.

The treatment is the same as in emphysema heart disease. Diffuse interstitial fibrosis resembles the subacute collagen disorders in some ways and steroid hormone may bring considerable temporary relief in some cases (6) but it does not cure.

1 Hamman, L., Rich, A. R. 1944. *Bull Johns Hopkins Hosp* 74, 177.
2 Rubin, E. *et al* 1952. *Ann. int Med* 36, 864.
3 Callahan, W. P. *et al* 1952. *Arch int Med* 90, 468.
4 Sloper, J. C., Williams, E. 1955. *Lancet*, 2, 533.
5 Arnott, W. M. 1955. *Brit med J* 2, 279.
6 Moore, F. H. *et al* 1957. *Arch int Med* 100, 651.

Pulmonary heart disease due to obesity. A curious syndrome comprising extreme obesity, cyanosis, somnolence, hypercapnia and ultimately right heart failure has been the subject of several recent reports. First described by Kerr and Lagen in 1936 (1) ...
acc ...
of ...
tio ... creased total lung volume, decreased functional residual capacity and decreased volume of expiratory reserve (3). Weight reduction and ...
dyspnœa and ...
one case (4) ... ickwickian syndrome" by Burwell *et al.* (5), because of the similar features described by Dickens in his famous fat boy, they describe a single case who showed the same features and developed cor pulmonale with failure. great weight reduction was also followed by loss of œdema, venous hypertension and hepatomegaly, even right bundle branch block reverted to normal conduction. A further two cases were

is due to the presence of multiple non-functioning air cysts up to 1 cm. in diameter, combined with interstitial fibrosis (The cysts do not communicate with bronchi in cases which are undoubtedly congenital (*1*).) The pathology in 66 cases has been recently described (*2*). Secondary cystic disease may be associated with eosinophilic granuloma, tuberculous bronchopneumonia treated with streptomycin, sarcoid, berylliosis and scleroderma. Pulmonary hypertension due to a relatively high resistance may produce the picture

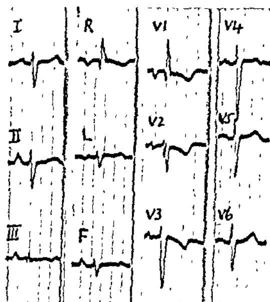


FIG. 66 Cystic lung disease causing right axis deviation and signs of great right ventricular hypertrophy in V1 and VR.

with the emphasis on hypertensive rather than hypoxic lung disease. We have seen such a case with a very high resistance (Fig 66) and Wood (*3*) records one with a mean pulmonary artery pressure of 43 mm Hg and a resistance of 10 units Such cases show considerable right ventricular preponderance on the cardiogram as in the case described by Bedford (*4*)

1. Norris, R. F., Tyson, R. M. 1947. *Amer. J. Path.* 23, 1075.
2. Heppleston, A. G. 1956 *Thorax*, 11, 77.
3. Wood, P. 1957 *Diseases of the Heart and Circulation* London, Eyre & Spottiswoode.
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Diffuse interstitial fibrosis of the lungs (*Hamman-Rich Syndrome*). It is uncertain whether this is a single disease entity as the

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Pulmonary heart disease due to obesity. A curious syndrome comprising extreme obesity, cyanosis, somnolence, hypercapnia and ultimately right heart failure has been the subject of several recent reports First described by Kerr and Lagen in 1936 (*1*) no further accounts seem to have appeared until several patients showing some of these features were described in 1955 (*2, 3, 4*) Respiratory function tests showed decreased total lung volume, decreased functional residual capacity and decreased volume of expiratory reserve (*3*) Weight reduction and venesection were followed by great relief of dyspnœa and œdema but hypoventilation and cyanosis remained in one case (*4*) This condition has been called a "Pickwickian syndrome" by Burwell *et al.* (*5*), because of the similar features described by Dickens in his famous fat boy, they describe a single case who showed the same features and developed cor pulmonale with failure great weight reduction was also followed by loss of œdema, venous hyperten-ion and hepatomegaly, even right bundle branch › normal conduction A further two cases were

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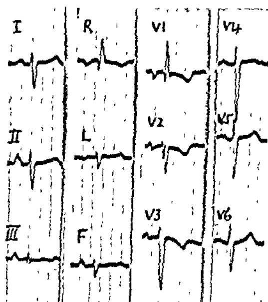


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Diffuse interstitial fibrosis of the lungs (Hamman-Rich Syndrome) It is uncertain whether this is a single disease entity as the

that severe secondary pulmonary hypertension from mitral disease and congenital shunts (Eisenmenger syndrome) produces a similar clinical picture of hypertensive pulmonary vascular disease, the features of which may entirely obliterate those of the underlying lesion The "purest" example of this condition is found in so-called idiopathic (solitary) pulmonary hypertension

IDIOPATHIC PULMONARY HYPERTENSION (SOLITARY PULMONARY HYPERTENSION)

The cause of this interesting and uncommon disease remains unknown. Many cases have been described and investigated during the past 20 years (*1-10*) This condition is a distinct disease, its

with pulmonary hypertension

PHYSIOLOGY AND PATHOLOGY The pressure in the pulmonary artery may be raised to the level of systemic arteries, the systolic pressure is often above 100 mm Hg (*11*) In one series the average was 111/59 (*8*) exercise produces a further rise of pressure. In the late stages of the disease pulmonary hypertension is lowered by right ventricular failure When the pulmonary capillary pressure can be measured it is found to be normal, but the pulmonary vascular resistance may be eight times the normal (*5*) with an average of 15 units (*12*) Normal wedge pressures and high resistance indicate that the obstruction is at a precapillary level. Indicator-dilution techniques show that there is a circulatory delay but no major shunt, although a small veno-arterial leak may occur through a foramen ovale, as shown by early appearance of dye in the systemic circulation after its injection at level of the venæ cavæ (*8*)

The pulmonary vascular resistance shows little tendency to change ...

... arterial oxygen saturation is normal but may fall slightly in late stages of the disease or, from secondary shunting of venous blood through a foramen ovale (8).

At necropsy the heart is heavier than normal because of right

described by Carroll (*6*) one of whom was examined at necropsy. Both had tremendous appetites and were grossly obese, their chests were relatively immobile and breathing was of the abdominal type. Heart failure associated with carbon dioxide retention and cyanosis occurred, and atrial fibrillation developed in one. At necropsy there was dilatation and hypertrophy of the right ventricle, the lung vessels were normal, there was terminal bronchopneumonia but no *emphysema or fibrosis. Two similar cases reported from the Mayo* Clinic (*7*) also demonstrated the great improvement which may be achieved by weight reduction, all the features of heart failure and albuminuria disappeared, high erythrocyte counts became normal and cyanosis disappeared. Primary cardiopulmonary disease due to obesity emphasises the adverse effects which obesity may have on patients who have other forms of heart and lung disease: existing dysfunction may be aggravated by the hypoventilation syndrome.

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HYPERTENSIVE PULMONARY VASCULAR DISEASE

This title includes various conditions in which a high pulmonary vascular resistance is essentially due to occlusive disease of lung vessels. The resulting obstructive pulmonary hypertension and right ventricular strain is similar to that produced experimentally by a variety of methods of occluding the pulmonary arterial system in animals. Pulmonary artery pressure may be of the same order as in the systemic circulation, causing right ventricular hypertrophy and secondary damage to the lining of the pulmonary arteries. The clinical picture is independent of its cause. Common symptoms are dyspnœa on exertion, anginal pain, cough and hæmoptysis, effort syncope, palpitation and hoarseness are less common. The signs are essentially those of pulmonary hypertension with peripheral cyanosis and varying degrees of right ventricular failure, slight jaundice is not uncommon.

Only those conditions in which pulmonary hypertension is primarily due to lung vascular disease, with or without parenchymal disease, are included here as pulmonary heart disease; but it is clear

that severe secondary pulmonary hypertension from mitral disease and congenital shunts (Eisenmenger syndrome) produces a similar clinical picture of hypertensive pulmonary vascular disease, the features of which may entirely obliterate those of the underlying lesion. The "purest" example of this condition is found in so-called idiopathic (solitary) pulmonary hypertension

IDIOPATHIC PULMONARY HYPERTENSION (SOLITARY PULMONARY HYPERTENSION)

The cause of this interesting and uncommon disease remains unknown Many cases have been described and investigated during the past 20 years (*1–10*) This condition is a distinct disease: its essential features are severe pulmonary hypertension due to occlusion *of the smaller vessels in the lesser circulation* without parenchymatous lung disease and any of the other usual abnormalities associated with pulmonary hypertension

PHYSIOLOGY AND PATHOLOGY The pressure in the pulmonary artery may be raised to the level of systemic arteries, *the systolic* pressure is often above 100 mm Hg (*11*) In one series the average was 111/59 (8) exercise produces a further rise of pressure In the late stages of the disease pulmonary hypertension is lowered by right ventricular failure When the pulmonary capillary pressure can be measured it is found to be normal, but the pulmonary vascular

niques show that there is a circulatory delay but no major shunt, although a small veno-arterial leak may occur through a foramen ovale, as shown by early appearance of dye in the systemic circula*tion after* its injection at level of the venæ cavæ (8)

The pulmonary vascular resistance shows little tendency to change on inhalation of 100% oxygen (8) pointing to fixity of the organic vascular occlusion; however, the injection of small amounts *of acetyl-choline* may cause a significant fall of pulmonary artery pressure suggesting that there is some pulmonary vaso-constriction in addition to organic obstruction (*12, 13*) The cardiac output is low and relatively fixed Arterial oxygen saturation is normal but may fall slightly *in late stages of the disease or*, from secondary shunting of venous blood through a foramen ovale (8)

At necropsy the heart is heavier than normal because of right

ventricular hypertrophy; an average heart weight of 393 grammes for 11 female cases was much higher than the normal of 250 grammes *(10)*. The pulmonary artery is dilated and the main branches often show gross intimal thickening and even atherosclerosis, but the most important lesions are in the small vessels where extensive



FIG 67 Primary pulmonary hypertension Pulmonary arteriogram shows obstruction of all small radicles of vascular tree giving the appearance of a "denuded shrub in autumn."

occlusion is well shown by means of post-mortem pulmonary arteriograms *(10)* The vascular tree looses its fine tracery and is replaced by a pruning of the lobular vessels and fine branches, giving the appearance of a denuded shrub in autumn (Fig. 67) When larger arteries are occluded by thrombus, anastomotic vessels may be seen and broncho-pulmonary communications are present On histological examination the most significant changes are in the small muscular arteries *(10)* where cellular material may occlude most of

the lumen by intimal proliferation: these changes are most conspicuous in regions where there is medial hypoplasia or aplasia. Many authors have described medial hypertrophy, but owing to varying degrees of post-mortem contraction Evans *et al.* (*10*) consider that hypertrophy cannot be identified with certainty. Further down the vascular tree the arterioles show varying degrees of intimal proliferation and sometimes complete occlusion, at any level there may be secondary thrombosis. Whether these abnormalities are primary or secondary in relation to the cause of high resistance, and consequent pulmonary hypertension, remains unknown.

CLINICAL FEATURES. The disease may be discovered at any age. All reports agree on the great preponderance of females: a point which may well have ætiological significance.

Dyspnœa is the commonest symptom. Orthopnœa and paroxysmal dyspnœa occur late in some cases. Pain in the chest on effort is common and indistinguishable from angina pectoris, it may be related to ischæmic changes which appear on exercise in the electrocardiogram (*14*). Effort syncope is also common, and probably due to acute right ventricular failure (*15*).

Patients who have developed symptoms usually show peripheral cyanosis; late in the disease a characteristic blotchy violaceous appearance is due to a combination of peripheral vaso-constriction from low cardiac output, high cutaneous oxygen extraction, polycythæmia and slight arterial unsaturation. The *physical signs* are essentially those of severe pulmonary hypertension from any cause: a small pulse, large "a" wave in the venous pulse, increased right ventricular pulsation and a palpable p[illegible]
tation there [illegible]
sound and [illegible]
heart failure [illegible]
heard over the right ventricle, is common.

Investigations help in two aspects of the clinical problem, firstly by confirming the severity of the pulmonary hypertensive disease, and secondly by exclusion of the other usual causes of pulmonary hypertension. The *electrocardiogram* shows unequivocal evidence of right ventricular hypertrophy and usually right atrial hypertrophy. *Radiological* examination shows the main pulmonary artery is dilated in every case and the main pulmonary branches are enlarged but the peripheral fields are ischæmic [illegible]
The aorta [illegible]

(Fig. 68). Splitting of second sounds is narrow and there is accentuation of the second component. An ejection click may mark the onset of a mid-systolic murmur over the pulmonary artery.

Cardiac catheterisation is an essential investigation if the solitary nature of the pulmonary hypertension is to be firmly established However, if the catheter tip does not enter an A.S.D., V.S.D. or P.D.A. a shunt cannot be excluded as blood gas analysis from right heart samples may not always reveal significant elevation of oxygen saturation from a left to right shunt. In cases where there is systemic

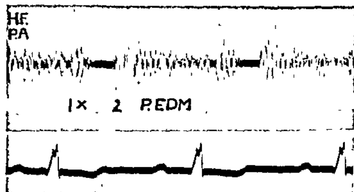


FIG. 68. Primary pulmonary hypertension High frequency phonocardiogram at pulmonary area (H.F P.A.). Shows pulmonary diastolic murmur (P.E D M) and ejection vibrations (X) in early systole

arterial unsaturation (due to a right to left shunt) the use of indicator-dye dilution techniques makes it possible to locate the site of the shunt In some cases although studies of blood oxygen saturation gave no evidence of an intra-cardiac shunt the technique of selective dye injection has demonstrated the presence of a ventricular septal defect (*8*) Cine-angiocardiography may be used to exclude right to left intracardiac shunting but the value of the method in the differential diagnosis of pulmonary vascular disease has not been fully assessed

PROGNOSIS AND TREATMENT *Once serious symptoms have* appeared the disease runs a rapid downhill course in most cases, but some increased breathlessness on effort may be noticed for many years before the final stage When the date of onset of symptoms can be firmly established the subsequent history lasts from 5 months to 7 years, the average is 2½ years (*10*) Pregnancy appears to be especially dangerous. No effective treatment is

known. The preponderance of organic vascular occlusion prevents vaso dilator drugs having any significant beneficial effect. Prolonged anticoagulant therapy has been suggested (*16*), but there is no evidence that it alters the course of the disease (*9, 12*)

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Schistosomiasis. It has been known for a long time that schistosoma infection may affect the lungs and cause pulmonary heart disease (*1, 2, 3, 4*) [illegible]
set up by the emboli [illegible]
S. mansoni may be [illegible]
pulmonary heart disease in areas where the disease is endemic and has been reported not only from Egypt but other parts of Africa (*5*) [illegible]

[illegible] ulmonary
[illegible] (*1*) those
[illegible] those due to allergy to ova and (*3*) those secondary to pulmonary hypertension The impacted ova become surrounded by proliferative arteritis, and new vessels form a local angiomatoid lesion Elsewhere in the vascular tree, where there are no ova, arteritis and hyaline thrombi may be seen, these lesions are possibly the result of allergy The severe pulmonary hypertension which develops is due to the very widespread obstruction which results from arteritis, angiomata and multiple hyaline thrombi

In Egypt young adult males are mostly affected, but in Puerto

Rico women are more often the victims. Extreme pulmonary [illegible]

from the pathology, is not uncommon.

X-rays may show a fine mottling over both lungs with oligæmia in the periphery which contrasts with large main pulmonary arteries. The electrocardiogram shows varying degrees of right ventricular hypertrophy. commonly the right chest leads show nearly monophasic R waves.

The disease runs a fairly rapid course and death usually occurs within two years of the onset of symptoms. As in other forms of pulmonary heart disease, superadded respiratory infection often precipitates failure

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Collagen disease. In acute hypersensitivity disease, polyarteritis nodosa, disseminated lupus, rheumatoid arteritis and scleroderma the lungs are often affected by pleuritis, miliary lesions, fibrosis and sclerocystic disease *(1)*, however, both anoxic and hypertensive pulmonary heart disease appears to be rare. In the development of cardio-pulmonary symptoms in collagen disease another factor is the frequent damage to the heart muscle by the primary disease.

In the histological examination of lungs from cases of pulmonary hypertension "arteritis" is sometimes described. in some cases it is clearly secondary to severe hypertension but in others it may be a primary vasculitis resembling the lesions of polyarteritis nodosa (2). Some cases of "eosinophilic lung" are associated with pulmonary hypertension due to a necrotising arteritis

Disseminated lupus erythematosus is rarely directly responsible for pulmonary hypertension dyspnœa and hypoxia are mainly due to pleural disease and mild pulmonary fibrosis

Polyarteritis nodosa may cause pulmonary hypertension (3, 4) However, as in other systemic collagen diseases, although lung damage is common, significant pulmonary hypertension is unusual.

Scleroderma may cause an obliterative arteritis of small vessels in the lung leading to a high pulmonary vascular resistance. However, dyspnœa and right heart failure are most likely to be the result of many factors including pulmonary fibrosis, cystic lung disease, pleural sclerosis, stiffening of the chest wall and myocardial sclerosis. It has been suggested that lung lesions are the result of bronchial arteritis and not primary pulmonary vasculitis (5).

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Metastatic carcinomatosis of the lungs. Multiple nodules may arise from malignant embolism (*1*) or by a spreading lymphangitis (2) In either case the vascular bed may be reduced by malignant occlusive arteritis, compression of arteries and arterioles, and by secondary thrombosis This may lead to subacute cor pulmonale with right ventricular enlargement (*1, 2, 3, 4*) Investigation of four cases of metastasis to the lungs showed that only one had pulmonary hypertension whilst the others were hypoxic from destruction of lung parenchyma (4) Wood (5) considers that diffuse *carcinomatosis of the lungs* mostly causes hypoxic cor pulmonale rather than obstructive pulmonary hypertension; one of his four cases had a pulmonary artery pressure of 45/20, a cardiac output of 7 5 litres/min and a pulmonary vascular resistance of only 2 units We have observed a case erroneously diagnosed in life as Hamman-Rich syndrome in which there was a hyperkinetic circulation and almost normal pulmonary function tests, and another due to *metastatic* chondro-sarcoma with severe pulmonary hypertension.

In a review of 178 cases of lymphangitis carcinomatosa approximately one-half of the cases were secondary to carcinoma of the stomach, the other common sites were bronchus, breast, pancreas and prostate (6)

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4 Storstein, O 1951 *Circulation*, 4, 913.
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PULMONARY EMBOLISM AND THROMBOSIS

Pulmonary hypertension may be produced in experimental animals by introducing foreign material or autogenous fibrin particles into the pulmonary circulation (*1, 2, 3*). It appears that at least 75% of the vascular bed must be occluded before significant overload of the right ventricle occurs; thus pulmonary hypertension does not follow from an isolated episode of pulmonary infarction, lobectomy or even pneumonectomy. The three possible effects of obstruction between the ventricles by embolism or thrombosis are: shock from a fall of left ventricular output, infarction of the lung and right ventricular failure from pulmonary hypertension (*4*). The clinical picture is determined by the size and frequency of embolism and modified by the presence or otherwise of secondary thrombosis. Massive embolism of the main pulmonary trunk causes acute cor pulmonale, whilst smaller and repeated emboli may lead to subacute or chronic hypertensive pulmonary heart disease.

Massive pulmonary embolism. The florid clinical syndrome of acute cor pulmonale comprises sternal pain, cyanosis, arterial hypotension and venous hypertension (cardiogenic shock) with gallop rhythm. Many patients, however, have milder attacks with slight signs and with less obvious symptoms such as apprehension, restlessness, irritability and only chest discomfort (*4*), transient faintness is not uncommon and is easily overlooked. The recognition of the significance of these lesser symptoms is important as they may precede further, and possibly fatal, embolism. The incidence of sudden death is probably less than generally realised; two-thirds recover, and the majority of fatal cases have survived hours or days after the initial episode (*5*). The survivors may succumb later to further embolism, or perhaps, more commonly, to extension of the occlusion by local thrombosis.

REPEATED SMALL PULMONARY EMBOLI may lead to subacute or chronic pulmonary hypertension (*6, 7*). The emboli are smaller than those responsible for acute cor pulmonale, but in such cases it is probable that local extension of the occlusion by thrombosis is a critical factor. Multiple emboli leading to extensive occlusion produces the clinical picture of severe hypertensive pulmonary vascular disease, which may be difficult to distinguish from idiopathic pulmonary hypertension, as there may not be a clear history of repeated lung infarction.

The electrocardiogram in acute pulmonary embolism. An analysis of 50 patients with pulmonary embolism shows that there are

patterns determined by acute right heart strain are first S_1, Q_3, T_3

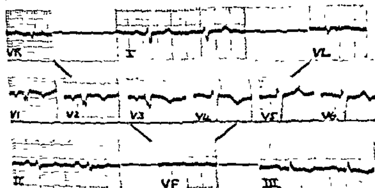


FIG 69. Massive pulmonary embolism Low voltage, S_1, Q_3, T_3 pattern and inversion of T waves from V1 to V4. At necropsy there was massive occlusion at bifurcation of the main pulmonary artery



FIG 70 Massive pulmonary embolism S_1, Q_3, Q_3 pattern Ventricular fibrillation followed a deep inspiration during recording (IIIR) Necropsy confirmation

appearance plus right ventricular T wave inversion, second S_1, T_3 or T appear...

The typical tall P wave of pulmonary heart disease is not common in acute embolism; it may appear for only a short time, but when present greatly strengthens diagnosis. S-T depression in left chest leads, presumably due to coronary insufficiency, may appear in the most seriously ill patients. Serial electrocardiograms are important in diagnosis as any of the abnormalities mentioned may be present for only a short time (*4, 8*).

Treatment. *Prophylaxis.* Early mobilisation [illegible] of tight [illegible] leg [illegible] freq [illegible] pat [illegible] should diminish the number of patients in whom pulmonary infarction is the first indication of phlebothrombosis Anticoagulant therapy is indicated as soon as thrombosis of the leg veins is detected and for all forms of pulmonary embolism

In *acute cor pulmonale* supportive measures are required during the phase of shock and failure The patient should be nursed flat and given oxygen therapy, pressor amine drugs if profoundly hypotensive and 10,000 units of heparin intravenously Morphine is contra-indicated but is occasionally necessary to relieve pain Digitalis may be given if the venous pressure remains high Anticoagulant therapy should be continued by one of the usual oral drugs until signs in the legs and lungs have disappeared for at least three weeks, thereafter the dosage of anticoagulant drug should be diminished slowly The position of surgical therapy has probably not changed from 90% mortality in 1939 because of the obvious practical difficulty of having a trained surgical team at the required place and time.

Massive thrombosis of main pulmonary arteries. This condition is relatively rare but several cases have been described recently (*9, 10, 11*) Pulmonary artery thrombosis mostly develops on previous embolism, but it occasionally arises *de novo.* Despite extensive chronic thrombosis pulmonary infarction is rather rare (*9*) preservation of lung is almost certainly due to the development of extensive broncho-pulmonary anastomoses. Chronic pulmonary disease is the most common pre-existing abnormality, but massive thrombosis may arise in any condition associated with pulmonary artery disease and pulmonary hypertension.

Dyspnœa is the common symptom; others are effort syncope, substernal pain, cough with occasional hæmoptysis and rarely mental confusion. The physical signs are those of a low cardiac

output from right ventricular failure, cyanosis is severe and mainly peripheral; murmurs are common over the pulmonary artery and may even suggest congenital heart disease where none exists (*11*).

The *radiological signs* are important The main pulmonary arteries are large and may appear "amputated" while the peripheral fields are oligæmic (12, 13) Evidence of past infarcts may be seen Fluoroscopy may reveal the absence of pulsation in the affected artery and angiocardiography shows a "filling defect." The *electrocardiogram* indicates varying degrees of right ventricular hypertrophy or strain depending on the duration of the occlusive disease.

Prolonged anticoagulant therapy offers the only way of preventing inevitable deterioration from progressive occlusion of the remaining channels

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10 Magidso
11 Ball, K *lation*, 14, 766.
12 Hanelin
13 Keating

The typical tall P wave of pulmonary heart disease is not common in acute embolism; it may appear for only a short time, but when present greatly strengthens diagnosis S-T depression in left chest leads, presumably due to coronary insufficiency, may appear in the most seriously ill patients. Serial electrocardiograms are important in diagnosis as any of the abnormalities mentioned may be present for only a short time (*4, 8*).

Treatment. *Prophylaxis.* Early mobilisation and the avoidance of tight bandaging in surgical patients, and less strict bed rest with leg exercises and early mobilisation in medical patients, diminish the frequency of thrombo-embolism. Frequent inspection of the legs in patients who are "vulnerable" should diminish the number of patients in whom pulmonary infarction is the first indication of phlebothrombosis. Anticoagulant therapy is indicated as soon as thrombosis of the leg veins is detected and for all forms of pulmonary embolism.

In *acute cor pulmonale* supportive measures are required during the phase of shock and failure. The patient should be nursed flat and given oxygen therapy, pressor amine drugs if profoundly hypotensive and 10,000 units of heparin intravenously. Morphine is contra-indicated but is occasionally necessary to relieve pain. Digitalis may be given if the venous pressure remains high. Anticoagulant therapy should be continued by one of the usual oral drugs until signs in the legs and lungs have disappeared for at least three weeks; thereafter the dosage of anticoagulant drug should be diminished slowly The position of surgical therapy has probably not changed from 90% mortality in 1939 because of the obvious practical difficulty of having a trained surgical team at the required place and time.

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Dyspnœa is the common symptom, others are effort syncope, substernal pain, cough with occasional hæmoptysis and rarely mental confusion. The physical signs are those of a low cardiac

exercise there is a much greater flow of blood to the periphery than normal The peripheral resistance is low. The systolic pressure is usually raised because of the enhanced force of the heart beat. Diastolic pressure may be low or raised, but these are casual pressures and not of much value in this disease. The pulse pressure is high, accounting for the bounding character of the pulse A "capillary pulse" in the small venules can usually be seen The rapid flow of blood leads to a decrease in the arteriovenous oxygen difference All these adjustments run parallel to the rise in the basal metabolic rate, and achieve extra dissipation of heat so that the temperature of the body, measured in the rectum, is kept constant In addition the extra demand of the tissues for oxygen is satisfied

Cardiac complications. When the disease is mild, especially in young women, the heart is unaffected, but in severe cases, or if the thyroid has been over-active for a long time, cardiac complications ensue They take the form of cardiac enlargement and auricular fibrillation and these lead easily to cardiac failure The average age of those who had heart failure in one series was fifty-one years (3). The patients with nodular goitres (Plummer's disease) were ten years older than those with diffuse goitres (Graves' disease)

CARDIAC ENLARGEMENT It is not very easy clinically to determine the size of the heart, for the increase in the force of the apex beat suggests enlargement When the symptoms are severe, or of long duration, skiagrams show a prominence of the left midcardiac segment, so that the left border becomes straight (Fig. 71) The outline thus becomes somewhat similar to that of mitral stenosis There is a difference in that the left ventricle may be enlarged too, so that the heart becomes like a ham in shape There is no enla[illegible]

[illegible] dilatation of the right ventricular outflow tract owing to the increased work needed to satisfy the requirements of the body for more oxygen

AURICULAR FIBRILLATION. Hyperthyroidism is an important cause of auricular fibrillation Auricular flutter is not uncommon The liability to fibrillate depends on the age of the patient, under thirty it is rare, but it is much more common in the elderly, most [illegible]

[illegible] the nodular variety

[illegible] the onset depends

CHAPTER 6

THE HEART AND CIRCULATION IN VARIOUS CLINICAL STATES

THE HEART IN HYPERTHYROIDISM

"There is one malady which I have in five cases seen coincident with what appeared to be enlargement of the heart . . . the malady to which I allude is enlargement of the thyroid gland" C. H. PARRY, 1825

Hyperthyroidism has a considerable effect on the heart and circulation The elevation in the basal metabolism produced by hyperthyroidism sets the activities of the body at a higher level, so that there is an increase in the demand of the tissues for oxygen This is met by increasing the flow of blood.

Effect on the function of the heart. The rate of the heart is increased and so is the cardiac output The tachycardia is persistent. There may be some slowing up during sleep, but even then the rate is always higher than normal The elevation of the sleeping pulse rate tends to be in proportion to the basal metabolic rate. The response in the rate of the heart to emotion and exercise is exaggerated and prolonged

Clinically, the abnormal force and vigour of the heart beat are familiar The sounds are loud, especially the first sound at the apex. In addition superficial scratching noises may be heard, usually at the third and fourth intercostal spaces to the left of the sternum These sounds appear to be produced in the pericardial sac by the abnormal vigour of the heart beat Soft systolic murmurs are often heard at the apex

/ **Effect on the peripheral circulation.** All the methods of estimating the circulatory rate agree in showing that this is fast The volume of the circulating blood increases (*1*) These changes appear to be associated with a larger cross-section of the vascular bed due to general vaso-dilatation Studies with a plethysmograph show that there is an increase in the average flow of blood to the fore-arm and leg at rest (*2*). More blood thus flows to the periphery making the skin flushed and warm This may be a means of eliminating the heat formed as a result of the raised metabolism After

tive symptoms may not be suggestive. The demeanour is jerky, and there is usually tremor. The skin is unusually warm and moist for an old person Cold is remarkably well tolerated, and but few bed clothes are required. Transient glycosuria may occur. The most constant signs are found in the cardiovascular system The fast bounding pulse and overaction of the heart are nearly always present An unexplained fibrillation is common Unless the diagnosis is made, these cases may progress to heart failure, for the elderly

Angina and hyperthyroidism. A masked hyperthyroidism may be present in some cases of angina pectoris. Exophthalmos and

whom it was performed, though the pain returned in some cases after a period of years, as would be expected in view of the progressive nature of ischaemic disease of the myocardium

Protein bound serum iodine In doubtful cases estimation of the protein-bound iodine may be of value The test is difficult to do since the amount present in the *serum is very small* No organic iodide, such as lipiodol, must have been taken previously The normal figures are 4–8γ for 100 *ml* of *serum* In hyperthyroidism the level is usually above 8, in hypothyroidism it falls below 4 (8) but there is considerable overlap and many hyperthyroid patients have normal figures while low values may be obtained where there

hyper-

satisfactory

As much of the gland as possible should be removed so as to leave the parathyroids intact A course of iodine therapy should be given for about a fortnight previous to the operation If the B M R is very high, this may be preceded by thiouracil for two or three weeks to lessen the activity of the gland The thiouracil should be discontinued before the iodine is

undue

is prese

will be

for elderly patients to have had a mild degree of hyperthyroidism for a long time Later the paroxysmal attacks are replaced by permanent fibrillation Hyperthyroidism causes about 7% of all cases of fibrillation. The attacks are often paroxysmal at first.

CONGESTIVE CARDIAC FAILURE. Most patients nowadays have a thyroidectomy before they reach the stage of cardiac failure. Out

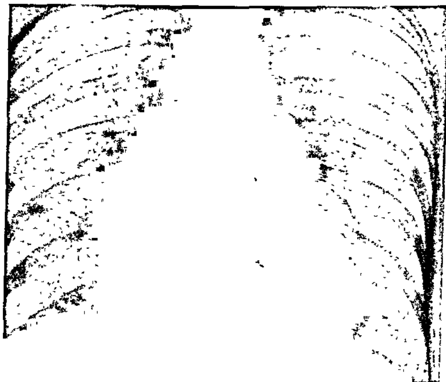


FIG 71 Heart in hyperthyroidism

of 130 patients in the U S A with cardiac complications one-third had congestive failure, and in nearly half of them normal rhythm was present, suggesting a severe grade of hyperthyroidism of short duration (6)

Masked hyperthyroidism. Hyperthyroidism in elderly persons may be overlooked These patients are less prone to show exophthalmos The eyes, nevertheless, may show some retraction of the lids and a peculiar stare, a "glittering eye" The goitres are often small, but the gland is hard and nodular, often it is mainly below the sternum. Loss of weight is invariable and most important. Subjec-

necessary first to determine the amount of protein-bound iodine present in the body. Traces of radioactive iodine (I^{131}) are then given and the uptake of the thyroid and the urinary excretion measured at the end of 48 hours. In 50 cases a dose of 160 micro- [illegible]

[illegible]

mined at intervals up to two months 38 of the patients became normal or myxœdematous in one to twelve months, most of them after one dose (*13*)

Radioactive iodine has also been used to treat patients with normal thyroids who had angina pectoris and congestive heart failure by making them hypothyroid (*14*) The required amount was given in three divided doses at fortnightly intervals Hypothyroidism was noted in from five weeks to five months Angina pectoris was abolished and congestive fail [illegible]

[illegible]

of the angina Small doses of thyroid extract were often required to control the myxœdema

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THE HEART AND CIRCULATION IN MYXŒDEMA

This subject provides an interesting contrast to the findings in hyperthyroidism Mild degrees of myxœdema are probably not uncommon, and the more severe types often escape recogn [illegible]

The onset of the [illegible]

dis [illegible]

the [illegible]

not [illegible] grees of hypothyroidism the clinical picture is familiar

and quinidine reserved until after thyroidectomy, otherwise there is a risk that fibrillation may return just before the operation and the rate will then be uncontrolled. The digitalis dosage will often require to be larger than is usual. Unless normal rhythm has returned spontaneously by ten days after the operation, a course of quinidine must be given since there is every prospect that it will succeed In severe cases a successful thyroidectomy depends a great deal on the judgment shown in selecting the optimum moment for the operation at the time of full medical control.

THIOURACIL. In young people with Graves' disease of moderate severity thiouracil may effect a cure. Formerly such patients recovered with prolonged rest and iodine, with thiouracil they do not need to rest. Thiouracil may also have to be employed in those who are unwilling to have a thyroidectomy. The usual dose of *Methyl thiouracil* is 400 mg daily, the latent period before improvement begins is about a fortnight The full effect is often accompanied by enlargement of the thyroid, which calls for a reduction to maintenance doses The only dangerous toxic reaction is agranulocytosis which is very rare, but comes on suddenly. The patient should be instructed to stop the tablets if he gets a sore throat, and to consult his doctor.

Propyl thiouracil is also available but offers no advantage over the methyl derivation The dose is 50–70 mg daily

Methimazole (1-methyl-2-mercaptoimidazole) has a somewhat similar structure to thiouracil, and was found to be a highly active anti-thyroid drug by Stanley and Astwood (*10*). The average dose is 5 mg three times daily with 5 mg daily as maintenance (*11*). No toxic symptoms were noted and enlargement of the thyroid does not occur during treatment Agranulocytosis has been reported, although it is rare as with the other anti-thyroid compounds Skin rashes may occur

Neomercazole (*Carbimazole*) is a very similar drug. Dose 10 mg. thrice daily

Potassium perchlorate has been recently introduced as a substitute for thiouracil since it has no toxic effect on the bone marrow It is ineffective if the level of iodine in the blood is high, such as when iodine has been given by mouth. The dose recommended is 400–800 mg daily If effective control cannot be gained by perchlorate alone, 10–20 mg. of thiouracil daily can be added (*12*)

RADIOACTIVE IODINE This method requires such elaborate and expensive apparatus as to preclude its use except in especially equipped centres Radioactive iodine is not given to patients with nodular goitres in case the nodules may be carcinomatous It is

necessary first to determine the amount of protein-bound iodine present in the body. Traces of radioactive iodine (I^{131}) are then given and the uptake of the thyroid and the urinary excretion measured at the end of 48 hours. In 50 cases a dose of 160 microcuries per estimated gramme of thyroid tissue was given The largest single dose was 15 millecuries, the largest total dose was 40 millecuries The B M R and the protein-bound iodine were then determined at intervals up to two months. 38 of the patients became normal or myxœdematous in one to twelve months, most of them after one dose (*13*)

Radioactive iodine has also been used to treat patients with normal ... stive heart failure by ... ed amount was given ... Hypothyroidism was noted in from five weeks to five months Angina pectoris was abolished, and congestive failure improved in rather more than half of the cases Sometimes a transient thyroiditis occurred in the early stages with pain and tenderness over the thyroid and exacerbation of the angina. Small doses of thyroid extract were often required to control the myxœdema

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THE HEART AND CIRCULATION IN MYXŒDEMA

This subject provides an interesting contrast to the findings in hyperthyroidism Mild degrees of myxœdema are probably not uncommon, and the more severe types often escape recognit... The onset of the ... disorder, toge... the patients ... more pronounced degr... of hypothyroidism the clinical picture is familiar

enough. The heavy, puffy, expressionless face; sparse, dry hair; dry skin; slow, dull mentality and croaking voice; somnolence, fatigue, and dislike of cold make an ensemble that should be easily recognised.

The circulation. When the basal metabolic rate is low, the skin is cold and dry. There is a decrease in the peripheral blood flow, per square metre of body surface per minute. As a result there is a diminished flow of blood to the skin (*1*). The capillaries themselves are affected. Microscopical study shows that only relatively few are open, and their loops are narrow (*2*) By means of the intravenous injection of fluorescine it has been possible to show that they are abnormally permeable, for an excessive amount escapes even though the number open are few (*3*).

The diminution of the flow of blood to the skin has the beneficial effect of conserving heat, which can ill be spared when metabolism is reduced It is the very opposite of the state of affairs in hyperthyroidism

The cardiac output is invariably low and the blood volume is usually diminished. Both these changes are related to the oxygen requirements of the tissues and, as these are low, the diminished supply is not harmful The opposite is the case in hyperthyroidism

There may be quite severe anæmia, simple hyperchromic, hypochromic, or Addisonian hyperchromic, the red cells ranging from two to three million (*4*) The reduced blood volume is not due to anæmia, however, since the plasma volume is also reduced (*5*) Nor does the anæmia play any part in the circulatory changes, since it would lead to a high output type of failure The cholesterol in the blood is high, and keeps fairly parallel with the basal metabolic rate

All these abnormalities will clear up under thyroid medication.

Cardiac lesions. No pathological changes have been found to account satisfactorily for the enlargement of the heart shadow which is present in all severe cases Ischæmic fibrosis is common; this is due to atheroma of the coronary arteries, to which the high level of the cholesterol in the blood no doubt makes the patient prone Macroscopically there may be moderate hypertrophy, and the muscle is pale and rather soft

Pericardial effusion. It has been claimed that a pericardial effusion accounts for the enlargement of the heart shadow In four cases straw coloured fluid was removed from the pericardium even though the shape of the cardiac outline did not suggest an effusion (*6*) In one of them the T waves became upright after the

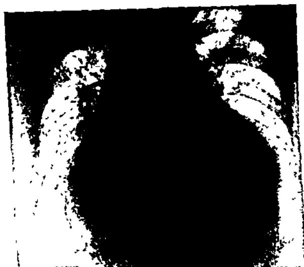


FIG 72 Pericardial effusion in myxœdema



FIG. 73 The same case after treatment

pericardial tap. The sluggish cardiac action, the feeble beat and the poor expansion on screen examination all favour an excess of pericardial fluid. The absence of tamponade might be due to the slow development of the effusion (Figs 72 and 73). Not all cases, however, can be explained in this way. Three pericardial taps were negative in one case. After treatment with thyroid the electrocardiogram returned to normal in six months by which time the patient had no symptoms, but the heart did not become normal in size for two years (7). It seemed here that the cardiac enlargement must be due to dilatation Hypertension is also not uncommonly found in association with myxœdema and this may cause some increase in size

Electrocardiograms. These are usually characteristic; P waves are small, there is a low voltage of QRS, and the T waves are

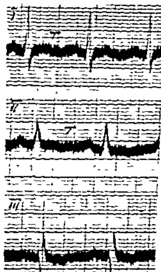


FIG. 74. From a case of myxœdema, showing flat T waves.

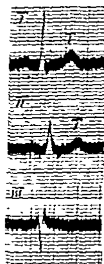


FIG. 75. From the same after taking thyroid, showing increase in T waves

flat or slightly inverted (Figs. 74 and 75). There may be slight slowing of auriculo-ventricular and intraventricular conduction Under thyroid medication these abnormalities tend to disappear in a few weeks. Their precise cause is uncertain They are very similar to the appearances found in pericardial effusion from other causes, and this no doubt explains them in those cases in whom an effusion is present. Another possibility is that the myxœdematous

skin has an increased resistance which lowers the potentials coming to the electrodes placed on it. In some cases anæmia may play a part An interesting point is that the changes do not occur in myxœdema induced by radioactive iodine, or by thiouracil

Congestive failure. This is very rare In most cases the arteriovenous oxygen difference is normal showing that the cardiac output, though low, is sufficient to meet the diminished needs of the tissues for oxygen In one case with orthopnœa and peripheral œdema, the venous, right ventricular and pulmonary pressures were normal, but the arteriovenous oxygen difference was high After treatment with thyroid normal figures were obtained (5) In another with angina pectoris the arteriovenous oxygen difference was also high, and in addition the mean pulmonary pressure and the ventricular diastolic pressure rose after exercise showing a temporary increase in pressure in the pulmonary circuit It seems that the low cardiac output is usually balanced by the sluggish metabolism, but sometimes the output falls below the level required by the body, and so more oxygen has to be abstracted in the capillaries giving rise to a raised arteriovenous oxygen difference

Myxœdema may complicate congestive heart failure from other causes [illegible] the œd [illegible] on the [illegible] increased [illegible] The heart also became much *smaller* The protein-bound iodine before treatment was low (8)

Angina pectoris. Angina pectoris may occur in myxœdema and some patients may be unable to tolerate any treatment with thyroid extract on account of increasing frequency of attacks (5). In others attacks may diminish greatly if thyroid is given *cautiously*, beginning with very small doses Angina pectoris appears to be associated with coronary disease which is independent of the myxœdema Thyroid extract may increase the efficiency of the heart and so improve the coronary *circulation* On the other hand the work of the heart is also increased The balance between these two results would seem to *determine* whether thyroid will reduce the liability to angina for a time, or will make it worse Patients with myxœdema may also have a dull precordial ache which is not cardiac in origin

Treatment. All observers agree that thyroid medication provides a cure in most cases But sometimes a patient who is very *far gone in the disease may fail* to respond The initial dose of thyroid may have to be very small, perhaps only half of a grain of the dry extract daily Otherwise there is a real risk that cardiac

infarction may be provoked. The dose can then be increased gradually up to 1½ grains daily, which is sufficient to control most cases

Apart from the possibility of associated coronary disease the prognosis is good If there is a liability to angina, a mild state of myxœdema is beneficial and should be maintained.

THE HEART IN INDUCED MYXŒDEMA. It is interesting to compare the effect on the heart of myxœdema induced by radioactive iodine with that of spontaneous myxœdema. *In nearly all of those* who gained relief from angina following the administration of radioactiv [illegible] *period of* [illegible] to most c[illegible]

The most constant finding in spontaneous myxœdema is some degree of enlargement of the cardiac shadow, due in many cases to pericardial effusion, and it seems as if either the grade of myxœdema is less when it is induced than when the disease occurs spontaneously, or there must be some essential difference in the reaction of the heart to the two types

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THE HEART IN ANÆMIA

In anæmia the capacity of the blood to carry oxygen is reduced. When this falls below a certain level for any length of time pathological changes occur in the myocardium and there are also profound abnormalities in the circulation

The critical level in the hæmoglobin below which these alterations become apparent is between 50 and 60%, or about seven grammes of hæmoglobin per hundred cubic centimetres

Changes in the circulation. These are adjustments which may be due to the demand *of the tissues for oxygen, and in a sense they* are compensatory to the decrease in the oxygen carrying capacity of the blood.

The cardiac output is increased *The rise in litres per minute* may reach double the normal level (*1*) This high level may be in

some degree associated with a tendency to an increase in the heart rate

The velocity of the blood flow is increased

At the periphery there is a decrease in the resistance (*2*). The pulse pressure is raised, so that the pulse is collapsing. Capillary pulsation can often be detected The skin is warm There is an increase in the arteriovenous oxygen difference, so that the percentage utilisation of available oxygen is raised (*3*).

... has been in a chronic state of severe anæmia for a ... some

the kidneys may be only half of the normal ...

of this sort, and by means of the increased utilisation of oxygen, these patients are able to maintain fair activity with low hæmoglobin values

Cardiac lesions. *Myocardial degeneration* The fatty degeneration of the myocardium has long been recognised in the post-... flabby The muscle ... reaks ... n may ... tients dying from gross and progressive anæmia and ... tment are seldom seen

CARDIAC ENLARGEMENT This was found in half the cases studied by Hunter (*6*) It is not related to the severity of the anæmia but rather to the amount of work done by the patient while anæmic In one series, where the patients were ambulant with parasitic anæmia, it was found in all (*4*) Following treatment the heart may diminish in size or even return to normal, but in some the enlargement persists *Pericardial effusions* have been described In one case, two pints were removed from the sac at autopsy, massive ... had been present for four years

of cases Some flattening of the T waves may be seen, or there may be a minor degree of heart block Depression of the RS-T junction may occur These changes may return to normal with improvement of the blood When cardiac enlargement persists, curves of left ventricular hypertrophy are recorded

Symptoms. When the hæmoglobin level is below 60% *dyspnœa* is common It was almost invariable in Hunter's cases (*6*), but he did not find orthopnœa and his patients could lie flat *Angina*

pectoris occurs in about one-third. The pain frequently disappears as the blood improves, and in some cases autopsies have shown no evidence of coronary disease. Others, however, consider that angina pectoris in anæmia always signifies some associated coronary atheroma and that the pain is only cured for a time (4) *Intermittent claudication* occurs occasionally.

MURMURS. Systolic murmurs are frequently audible. They vary in intensity and are heard most often at the apex, next in the pulmonary area and least often in the aortic area (6). They go when the blood returns to normal. Rarely a basal diastolic murmur can be heard This is probably due to pulmonary incompetence We have heard it only in severely anæmic patients who have been ambulant in spite of enlargement of the heart and of the pulmonary artery Under treatment the diastolic murmurs disappeared and the pulmonary artery became normal in size at about the same time

HEART FAILURE. If a severe anæmia complicates some form of heart disease such as mitral stenosis, hypertension or hyperthyroidism, *congestive failure is likely to come on. Unless the anæmia* is recognised and treated, the failure will not respond

When the hæmoglobin value falls below $20\%_0$ and the red cells number less than a million and the patient is still ambulant, as formerly occurred in pernicious anæmia, breathlessness on exertion is extreme, and orthopnœa is present. A right ventricular gallop may be heard and the pulmonary artery enlarges The veins in the neck are congested Œdema is present although hypoproteinæmia may be a factor in this (8) All these features disappear if the anæmia is successfully treated These cases are not encountered under modern conditions and it is doubtful whether, with their exception, anæmia alone can cause true congestive failure

In severe chronic anæmia with signs of congestion the low renal flow increased up to *200%* after treatment Since the cardiac output fell at the same time, there must have been a very large increase in the fraction of the blood passing through the kidneys It is suggested that the œdema and raised venous pressure may be due to retention of water caused by renal anoxia (1) •

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CHAPTER 7

DISEASES OF THE CORONARY CIRCULATION

MYOCARDIAL INFARCTION

Incidence

MYOCARDIAL infarction and its relation to coronary occlusion was well recognised before the First World War; but it was rare. The records of the pathological department of the London Hospital show that an average of two such necropsies occurred annually The incidence began to increase in 1917 which was some years before the condition was generally recognised clinically (1) Since then the increase has been progressive, in 1956 75,000 deaths were registered from coronary heart diseases, compared with 30,000 in 1946 Even when due allowance is made for an ageing population, readier diagnosis, and for the replacement of "myocarditis" by "coronary thrombosis" in death certificates, this incidence constitutes a major problem in medicine today

Age and sex. Men are more liable than women by four to one. Up to the age of 50 years the ratio is seven to one The peak period for males is between 55 and 60 in women the incidence rises steadily up to 70 years (3)

Coronary atheroma. At the London Hospital atheroma of the coronary arteries is graded according to the degree of calcification present Using this as a measure of advanced atheroma it was found th...

... and thrombosis (2)

Thrombosis and arteriosclerosis. Old thrombi which are becoming canalised contain fibrous tissue which merges with the intima, and gives the appearance of intimal thickening Mural thrombi may occur frequently, due to some thrombogenic influence and cause the thickened vessels of atherosclerosis (4) Feeding rabbits with cholesterol leads to foam cells being deposited on the intima and these may become covered by the intima and so cause the plaque Localised collections of fat containing phagocytes are

often seen at the edges of old intimal plaques. The plaques may increase in size by replacement with fibrous tissue of these fatty deposits (*5*). The presence of atherosclerosis does not necessarily involve impairment of the coronary circulation; it is possible that spasm is a factor (*6*). Discrete foci of round cells forming a perivascular collar round the vasa vasorum of large coronary arteries were found in 80% of those dying from infarcts, and also in deaths from asphyxia such as cerebral hæmorrhage or hanging where spasm is likely to have been present (*7*).

Influence of cholesterol. In samples taken from populations with a high rate of coronary disease the serum cholesterol averaged more than 220 mg. whereas it was 150 mg. in areas such as Sardinia, and the native quarter of Cape Town where the incidence is low (*8*) Successes have been claimed for a diet low in fats in the long-term treatment of infarction. 50 cases took only 25 g of fat daily for eight years, and half were living at the end of that time compared with one-quarter of those who ate a normal diet (*9*). After four weeks of treatment with the rice diet of Kempner the stickiness of the platelets diminished, as well as the level of the serum cholesterol, in patients with ischæmic heart disease (*9A*) On the other hand the considerable variation in the death rate from infarction in countries with a similar high intake of fat makes it obvious that this is not the only factor. Thus the mortality in Denmark is half that of Finland or New Zealand and that in Stockholm half that in Edinburgh (*10*)

THE PHOSPHO-LIPIDS. *Attempts have been made to incriminate a fraction of the cholesterol* The alpha and beta lipo-proteins are those portions of the cholesterol which are attached to proteins. The amount of cholesterol attached to the alpha fraction was found to be decreased in men with coronary disease and especially in younger men under forty (*11*) It is suggested that cholesterol attached to protein as lipo-protein may not be deposited on the intima. In women this decrease in the alpha fraction does not occur and the incidence of infarction in females is less than in males at all ages, and occurs later in life (*12*). Paper electrophoresis has shown another band, the "pre beta lipid pattern," in patients with recent infarcts. This pattern is absent in normal women and in men under 30 years, but is present in moderate amounts in most men over 50 years It is not increased beyond the normal for age in patients with healed infarcts, nor in those with hypertension or arterial disease. In infarction the increase takes place after the first few days and reaches a maximum in about four weeks (*13*) Ethinyl

œstradiol ·4 mg daily reduced the plasma cholesterol without effecting the lipo-protein, and it may be that women are protected in some measure up to the time of the menopause by hormones (*14*)

Using the method of gas-liquid chromatography no difference was found in any fatty acids between patients with coronary disease and controls of similar age There was a slight increase in one unsaturated fatty acid (abeic) compared with the saturated form (steric) (*15*)

Triiodothyroacetic acid reduced the plasma cholesterol level in men with healed infarcts and hypercholesterolæmia, but also reduced the phospho-lipids There was an increased tendency to angina since the oxygen requirements were raised (*16*) *Sitosterol*, a plant

A similar effect was noted with *inositol* (*18*) A diet with a high proportion of oil rich in fatty acids such as soya-bean oil has been found to lower cholesterol levels. Lard, *animal fats*, white bread and cereals are not allo

th

tu

af... a fatty meal in patients with healed infarcts than in normal people Intravenous heparin in doses of 25 mg. reduced the level of the lipæmia (*20*) A polysaccharide from seaweed—laminagin sulphate

... higher than normal in those who have had cardiac infarction, and that populations whose dietary habits lead to a low cholesterol level are relatively free from the disease But there are wide variations in the incidence of infarction between countries who have a similar high intake of fat

STRESS In middle age the *mortality* in men is five times that in women, and it is particularly high in business men, doctors and other professional workers It is suggested that the stress of modern life, combined with the more sedentary conditions promoted by the motor car and the telephone may be among the causes of this increase (*22*).

HEREDITY As in the case of hypertension there is a strong hereditary factor A history of death from cardiovascular disease

in one or other parent can be obtained from half of those with infarction

Influence of climate. In a climate where summer temperatures often exceeded 100°F the highest incidence of infarction occurred during these months (23) A sudden change to cold weather also made these more frequent (24)

Urticaria. A curious association with urticaria has been found in a few cases. Three patients had injections of penicillin in oil and developed urticaria. The T waves became negative in several leads (25). The curve returned to normal in about a week. Another received anti-tetanic serum and a week later had serum sickness with urticaria and precordial pain which was due to a transmural antero-septal infarct (26). We have seen a man who became dyspnœic four hours after the onset of generalised idiopathic urticaria and had a subepicardial antero-lateral infarct. The curve returned to normal in a fortnight

Associated diseases Congenitally aberrant coronary arteries may become occluded. One young soldier with two left coronary arteries died suddenly, when one was blocked by an atheromatous plaque (27). An association with diabetes is present in 10% of cases. Infarction may occur in polycythæmia vera, polyarteritis (28) and porphyria (29)

The Coronary Circulation

The coronary arteries vary in their size and distribution. In 40%, the left coronary, dividing into the anterior descending and circumflex branches, supplies the whole of the left ventricle, while the right coronary supplies the right ventricle In another 40% the right coronary supplies also the posterior part of the left ventricle; while in the remaining 20% a considerable part of the right ventricle is supplied by the left coronary The coronary arteries are not, strictly speaking, end arteries, since fine communications up to 40μ in diameter exists between them in health (30) These collateral branches increase in size greatly when one of the main arteries is narrowed, so that much of its territory may come to be supplied by branches from the other. In about one case in four the anterior descending artery lies buried in heart muscle for varying distances Few of these stretches showed any atheroma and it appears that contraction of the muscle protects against undue distension of the artery (31) In 50% a *conus artery* arises from the aorta behind the right aortic cusp and supplies the pulmonary

conus It is seldom occluded and may serve as a source of anastomatic blood supply (32) to the coronary circulation

Myocardial infarction. Cardiac infarcts usually follow the occlusion of a coronary artery and the size of the infarct depends upon the point at which the vessel is blocked. An abrupt occlusion of the orifice of a coronary artery will lead to the death of so large a part of the myocardium that fatal heart failure is inevitable Occlusion of a small branch may pass unnoticed or cause trivial symptoms which the patient ascribes to indigestion Infarction may also occur without the occlusion of a coronary artery in patients with large hearts in which the blood supply by reason of the hypertrophy is relatively insufficient

CARDIAC INFARCTION WITHOUT OCCLUSION *Coronary insufficiency* is a term that has been used somewhat loosely to describe a clinical state in which there seemed insufficient evidence to postulate a coronary occlusion although the electrocardiogram showed ischæmic changes. Most of these cases have had small infarcts and it is the injured muscle or the fibrosis which causes the cardiographic abnormalities It is better to diagnose infarction or ischæmia. In aortic stenosis where the left ventricle is hypertrophied and the aortic pressure is low, a portion of the myocardium may become ischæmic and an infarct may result Other predisposing factors are chronic congestive failure and stenosis of the coronary *ostia* (33) Precipitating factors are associated with a fall in blood pressure and include severe hæmorrhage from the gastro-intestinal tract (34), prolonged tachycardia and pulmonary embolism (35) Infarction may also occur after operation, especially in patients with pre-existing cardiovascular disease In one series of twenty-five cases seven occurred on the day of the operation and sixteen more within one week (36)

Mechanism of coronary occlusion. In almost all cases the occlusion is due to a final thrombosis of the artery, but in many the thrombosis is secondary to a capillary hæmorrhage In normal hearts vasa vasorum are only present in the adventitia of the coronary arteries . . .

. . . from the vasa vasorum, but may grow in from the lumen of the vessel The new capillaries are fragile and liable to rupture, and the artery then becomes narrowed by the resulting hæmatoma, or by the extrusion of the atheromatous plaque into the lumen through the pressure of the hæmatoma forming behind

it. A thrombus forms easily on the sticky surface of the protruding hæmatoma or atheromatous debris, and so secondary thrombosis completes the occlusion of the vessel *(37)*. In other cases an atheromatous plaque becomes detached and is swept along the vessel to block it lower down. On rare occasions an embolus, such as a fragment from a vegetation in bacterial endocarditis *(38)* or from an endocardial clot, may enter a coronary vessel and obstruct it. Thrombi round the aortic cusps in syphilitic aortitis have done so very rarely *(39)*.

SITES OF INFARCTION. Myocardial infarcts are practically confined to the left ventricle, although a large infarct may extend across the septum to involve the right side as well. *Antero-septal* and *antero-lateral* infarcts follow occlusions of the anterior descending branch of the left coronary. *Posterior* and *postero-lateral* infarcts result from occlusions of the right coronary or the circumflex branch of the left. Occlusion of the circumflex branch sometimes gives rise to an infarct limited to the free wall of the left ventricle—the *lateral infarct*. Infarcts may occur principally in the septum when they frequently cause defects in conduction. A large infarct may involve both the anterior and posterior walls—the *antero-posterior* infarct. A *papillary muscle* may be infarcted, and lead to mitral incompetence, perhaps with fatal results.

Infarcts are also divided into the *transmural* in which the whole thickness of the ventricular wall is affected, and the *subepicardial* and *subendocardial* types.

These types can be distinguished in the main by the electrocardiograph.

Infarction at a distance. When there has been progressive narrowing of one coronary artery, the collateral circulation may develop to such an extent that the muscle in the territory of the diseased artery may come to be supplied by the other. Thus, after narrowing of the anterior descending branch of the left coronary, the region at the apex may have to rely for its blood supply upon collaterals from the right coronary, and occlusion of this artery may then cause an anterior infarct.

RELATION OF CORONARY OCCLUSION TO CARDIAC INFARCTION. It was formerly thought that, if narrowing of a coronary artery had progressed slowly, the final occlusion would not result in an infarct *(30)*. Recent work with improved technique has not confirmed this view. Only four occlusions out of forty were found not to be accompanied by an infarct, and in each the artery had been previously occluded so that the blood delivered by it would, in any case,

be small (40) In other cases patchy fibrosis confined to the subendocardial zone was found, the appearances being those of subendocardial infarction. These patients had suffered from severe angina but had never had prolonged pain. They had narrowing of the coronary ostia and severe coronary disease Arteriograms showed a network of small vessels in the subendocardial zone, and the fibrosis in this zone, which is furthest from the blood supply, was probably due to prolonged myocardial ischæmia (41)

The infarct. After five hours the nuclei of the muscle fibres are pale and swollen After fifteen hours the infarcted area is pale and œdematous [illegible] be seen on th [illegible] necrosis has t [illegible] and grey Leucocytic infiltration begins in six hours and is at its height in four days At this time proliferating capillaries appear round the border, reaching their maximum in three to eight weeks. In three weeks the wall tends to become thin Fibroblasts can be seen by the fourth day, infiltrating the infarct which by three months has become firm and white Collagen fibrils which consolidate the scar begin to appear by the ninth day It is possible to date an infarct almost to a day during the first week, and to seven days in the first eight weeks (42)

The inner surface of the ventricle is usually more extensively involved than the outer, but a thin layer of muscle commonly survives immediately beneath the endocardium, being nourished either by the Thebesian veins, or directly from the blood in the ventricle If the infarct reaches the pericardium, pericarditis results and adhesions, usually thin, may form, or merely an area of thickened epicardium results On the inner surface of the infarct a mural thrombus may form · mural thrombi begin to organise at the ninth day after infarction, and organisation is complete by the sixteenth day (43)

CARDIAC RUPTURE Spontaneous rupture of the softened area may occur, causing hæmopericardium and sudden death Rupture of an infarct takes place most often during the first week When the fibrous area is large, an aneurysm of the left ventricle may be produced Occasionally the infarct becomes calcified

HEALING OF INFARCTS The time which an infarct takes to heal will depend upon its size. Small infarcts heal almost completely in a month Large infarcts usually heal in two months, though islands of necrotic muscle may persist for many months Extensive recanalisation of the thrombosed artery may take place

Clinical Syndrome of Cardiac Infarction

Prodromal attacks. Preliminary attacks of substernal pain during the month or so before the occlusion occur in about a third of all cases (*44*) The attacks may come on exertion and so simulate Heberden's angina although the pain may outlast the exertion Less frequently they occur at rest, lasting half-an-hour or more They have a certain crescendo quality occurring more frequently and more severely as the moment of the infarction approaches. They are uninfluenced by treatment and the electrocardiogram is normal unless a record is taken while the pain is present. These prodromal symptoms are probably related to the initial capillary hæmorrhages and hæmatoma formation. Spasm of the artery may play a part

The infarct. ONSET Since in most cases the final occlusion is due to secondary thrombosis, exertion plays no part in determining the onset Three-quarters of all attacks occur at night or during mild activity in the day. Sudden death may result when a large trunk is occluded, but death may also come suddenly to patients who have not rested at the onset because their infarcts caused no symptoms. Death here may be due to ventricular fibrillation or standstill Animal experiments suggest that the reflex coronary vasoconstriction may play a part But the great majority of patients survive the onset, and experience a triad of symptoms comprising pain, dyspnœa and collapse. In severe cases these are usually all present together in varying degree, in milder attacks collapse is commonly absent.

Pain. Pain is the most arresting symptom, and occurs in the large majority. The patient may experience anything from intense agony to a dull ache The sensation is described as rending, tearing or crushing The site of the pain is usually substernal, and occasionally epigastric From here it may radiate down the arms or up to neck, jaws and teeth Occasionally the pain starts at some other point such as the throat or back and spreads to the sternum later With the intensity of the pain the patient cannot keep still, he may writhe in agony or walk about. There is no relief in immobility, as in agina of effort In milder cases the patient invariably says "I thought it was indigestion" particularly if not dyspeptic.

DURATION. The pain may last from half-an-hour to several days, unless controlled by morphia After the worst is over a dull ache may persist for a long time Sometimes the pain is of the waxing and waning variety, causing successive attacks

DYSPNŒA This is present in all severe attacks, though frequently

masked by the pain * It is due to left ventricular failure which may progress rapidly to acute pulmonary œdema, beginning with a short dry cough In fact, myocardial infarction should be suspected if a patient develops an attack of pulmonary œdema which cannot be explained satisfactorily on other grounds.

COLLAPSE In severe attacks the patient suffers from shock. He is both pale and cyanosed with a greyish colour The extremities are cold· sweating is common He is prostrate and apathetic, but the mind is clear These are signs of peripheral circulatory failure; but the venous pressure in infarction is normal or raised, and pulmonary congestion is invariable, and may sometimes reach a severe degree indicating a central failure with a low ventricular output. The pulse is small, weak and fast as a rule Although the pulse pressure is small, the diastolic pressure is not so low as in pure peripheral failure, as a rule

It is difficult to say how far the signs in the peripheral circulation are due to shock, or to gross deficiency in the output of the left ventricle There may be two types, the first comes early with but little dyspnœa, and is due to peripheral vasomotor collapse, the second comes later, dyspnœa is prominent and cardiogenic in origin. [illegible] rtality

[illegible] mark

[illegible] pointed out in 17[illegible] (syncope anginosa) The patient may be unconscious, or semi-conscious, but convulsions do not occur (16) As consciousness returns pain is felt The [illegible]

BLOOD PRESSURE The blood pressure usually falls, and always does so if there is collapse In patients with hypertension the systolic pressure may drop more than 100 mm of mercury. the diastolic remains relatively high In the early painful phase the blood pressure may actually rise temporarily to a considerable degree

PULSE The pulse is not much quickened unless shock or left ventricular failure are present when it is small and weak Acceleration to above 100 beats per minute increases the gravity of the prognosis In some cases the rate is rather slower than usual.

Physical examination. Physical signs at the heart in the early stages are inconspicuous The first sound at the apex may be weakened and the sounds may be evenly spaced A gallop rhythm may occasionally be detected, more often in hearts enlarged as the

result of *hypertension*. The pulmonary second sound may be accentuated. In a few cases of transmural anterior infarction an expansile pulsation can be detected *internal to the* apex during the first week (*47*), and the heart beat may be *double*.

PERICARDITIS. Although localised pericarditis is common, pericardial friction is heard only in a small minority of cases, and it is evanescent. [illegible] Localised pericarditis c[illegible]n anterior infarcts, but in a small proportion of recent infarctions a general pericarditis has been found (*48*), so that friction may on occasion be heard with a posterior infarct.

FEVER. After an initial phase when the temperature is subnormal, fever occurs in the majority of severe attacks at some time between the second and fifth day The height of the temperature and the duration of the fever are useful guides as to the prognosis Prolonged fever is rare, and is likely to be due to complications such as pneumonia

LEUCOCYTOSIS. A moderate leucocytosis is common, commencing very soon after infarction. In uncomplicated cases the count does not usually rise above 15,000 *per cm*

SERUM TRANSAMINASE. The serum *glutamic oxalacetic transaminase* (serum aminopherase) is especially concentrated in heart muscle Normal limits in the serum range from 10–40 units. After an infarct the concentration rises to 50–500 units, the extent of the rise depending upon the size of the infarct In fifty transmural infarcts the average figure by the end of the first day was 200 units The concentration had returned to normal in ten by the third day and in all by the seventh (*49*).

The serum transaminase is increased in hepatitis but not to the same extent as in infarction, and the rise is more prolonged. It is also raised in other conditions associated with injury to the tissues but is normal in congestive failure, dissecting aneurysm and rheumatic heart disease unless there is active myocarditis It was normal in twenty cases of angina and slightly raised in four, suggesting small areas of necroses (*50*).

THE ERYTHROCYTE SEDIMENTATION RATE rises about the third day, and remains high for about a fortnight It usually returns to normal by the end of a month

Plasma fibrinogen. The E.S R may fail to rise if hæmoconcentration is present. In these cases the plasma fibrinogen is more accurate In three cases of massive infarction the E S.R was normal when the hæmatocrit was fifty-two, but the fibrinogen was raised

from the normal value of 250–400 mg to 460–750 mg (51). The daily excretion of *coproporphyrins* in the urine has been found to increase from the normal limit of 140 microgrammes to 200–300 microgrammes during the first few days after an infarct. They returned to normal in the second week. They were also increased after a pulmonary embolism (52).

Diagnosis

Recent cardiac infarction. CLINICAL In many cases the diagnosis presents no difficulty Prolonged substernal pain occurring at rest accompanied by sweating and grey cyanosis in a patient with a history of recent anginal attacks is unlikely to be due to anything but a cardiac infarct Many others, however, do not conform to this classical pattern Prolonged pain occurred in 70% of those in whom infarction was due to an occlusion of a vessel, but only in a third of those who had a recent infarct but no occlusion (53) The remainder had either angina of effort, or dyspnœa at the onset, or else they had no symptoms at all Conversely, out of 60 cases of angina confined to effort, half had electrocardiographic evidence of infarction (54) That infarcts may be painless has for long been known (55) The cause may be a long ischæmia of low intensity These painless infarctions are liable to complicate the course of congestive failure. In others the attacks may be mild, and the painful phase not prolonged, or the pain may wax and wane and the patient may seem to have a succession of attacks of angina pectoris Sudden dyspnœa with pulmonary congestion, or pulmonary œdema, may take the place of pain Finally the onset may not be remembered by the patient, who may come under observation for a complication such as cerebral embolism

Changes in the electrocardiogram. Changes in the electrocardiogram following myocardial infarcts comprise the appearance of Q waves, elevation or depression of the RS-T junction and negative T waves

Q waves Active heart muscle is electrically negative to inactive muscle The impulse reaches the ventricles through the A-V bundle which runs in the subendocardial zone. It spreads almost at once to the ventricular cavities, which are therefore [illegible]

[illegible]

[illegible] through the ventricular wall to the epicardium the charge in front of the advancing face will be positive

Since the electrical changes reach the surface of the body through the epicardium, and chiefly reflect the condition of the subepicardial muscle cells, the major initial deflection of a normal QRS is positive If, however, the muscle cells have died as the result of infarction, there will be nothing to prevent the negative potentials of the cavity reaching the surface It is as if a window had been cut through the ventricular muscle (*56*). The initial deflection will then be negative, and deep Q or QS waves will appear. This will be seen best when the electrode is placed directly over the infarct as in precordial leads in anterior infarction. In the precordial leads, in the absence of right ventricular hypertrophy, the voltage of R should increase as the electrode is moved from right to left A diminishing R wave under these circumstances also signifies an anterior infarct in most cases.

Q waves are considered pathological when they have a duration of more than 0 02 sec from onset to nadir, and have a voltage of more than a quarter of that of the succeeding R. Alternatively a normal Q wave, if it is followed by an R wave the upstroke of which is notched and prolonged beyond 0 06 sec, also usually signifies infarction (*57*).

Although these criteria are in general well founded, a Q wave in lead F of more than 0 04 sec from onset to nadir was also found in 7% of a large group of normal subjects, while 20% had Q waves with a voltage of more than a quarter that of the R wave (*58*)

RS-T displacement Surrounding the central core of dead muscle in an infarct, is a zone of muscle injured as the result of being cut off from the blood supply Injured muscle emits a constant negative current. This current is neutralised along with the skin currents in diastole by the compensating mechanism embodied in the instruments In systole, however, the whole myocardium is active and so negative, and no current then flows from injured to uninjured muscle. The neutralising current from the compensator is released and causes a deflection of the fibre which gradually terminates as more and more of the muscle passes into the resting state The direction of this deflection depends upon the position of the injured area in relation to the epicardium If the damage is anterior and involves the epicardium, a negative current will reach the skin under the electrode, and the neutralising current which is released during systole will be positive Therefore, upward (positive) displacement of the RS-T in precordial leads and in lead L will result If the injured area is in the subendocardial zone, it will be the positive reaction of the intervening uninjured muscle which will reach the skin The neutralising current will then be negative

downward, or negative, displacement of RS-T will occur. In the reciprocal leads, which face the tail of the wave as it advances through the infarcted area, the displacement is downward. Thus downward, or negative, displacement of RS-T is found in the precordial leads in a recent posterior infarct, in an anterior infarct the displacement is downwards in F and in lead III. This only occurs when the muscle whose potentials are reflected to the surface by these leads is uninjured. If multiple infarcts are present, such as a recent anterior and a healed posterior infarct, or vice versa, depression of the S-T segment does not occur in the reciprocal leads

The current of injury is usually a transient phenomenon. the cells either die, or recover to become only ischæmic. Rarely the upward displacement of RS-T in the precordial leads persists The reason for th...

epicardial muscle cells ... to the in...
subepic
Nega
ischæm
T wave ... A negative T wave is the first change to be seen *following* the experimental occlusion of a coronary-vessel, elevation of the RS-T junction comes later. After release of the vessel the inversion of T is the last abnormality to disappear *(60)* The *same sequence* can be observed in records taken during prodromal *attacks* (Fig 76) Negative T waves are caused by delayed repolarisation, and indicate that the muscle is recovering imperfectly They can be produced by cooling the precordium in thin *people (61)* ...
dial disease,
characteristic
an early up... ... or else the fibre moves upward in a straight line followed by a sharp dip—the plateau type, or T is deeply negative. The T wave may reach a depth of 30 mm in precordial leads (62) *Deeply negative* T waves may also occur after paroxysms of ventricular tachycardia Otherwise they are due to subepicardial ischæmia (63) Bradycardia may play a part

Precordial leads. In a joint memorandum issued by the British Cardiac Society and the American Heart A...

The precordial electrode is placed on certain relatively fixed positions on the chest; the points are numbered from C1 to C6 and are obtained as follows: C1 is at the right margin of the sternum in

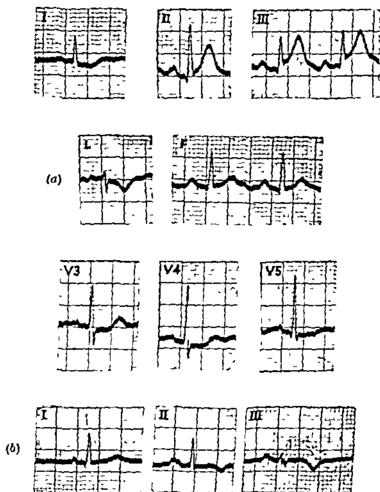


FIG. 76. (a) Record taken during prodromal attack showing elevated ST junction in leads II and III and depressed ST junction in leads I, L, V3–V5 (b) Record taken 15 mins later, after cessation of pain showing persistence of negative T waves in leads II and III when other changes have returned to normal.

the fourth intercostal space. C2 is at the left margin of the sternum in the same space; C3 is midway between the left margin of the sternum and the mid-clavicular line in the intercostal space in which

lies the apex, C4 is at the mid-clavicular line in this space; the C5 and C6 are at the anterior and mid-axillary lines at the same level. Thus the first two positions are fixed, while the remaining four vary in regard to their horizontal levels according to the space in which the apex lies If desired C7 in the posterior axillary line may be included C3R and C4R denote corresponding leads to C3 and C4 in the right hemithorax. Leads may also be taken along the third space and are then registered as C3 (3rd space), etc.

V LEADS Formerly either the right arm (CR) or the left leg (CF) were used as the indifferent electrode, but these leads have been superseded by the "V" lead technique of F. N. Wilson which is now in general use throughout the world The three limb leads are connected through resistances to a central terminal which is used as the indifferent electrode Einthoven postulated that the algebraic summation of the potentials at all three points on his triangle in the horizontal plane at any given moment in the cardiac cycle is zero This does not include potentials generated in the antero-posterior plane but these are very small. There is no doubt that "V" leads are the most accurate precordial leads available, and they avoid the distortion which occurs in some records from potentials derived from the right arm or left leg Modern instruments include a "V" connection It is customary to designate these leads simply as V1 to V6

UNIPOLAR LIMB LEADS The standard leads are bipolar. Lead I expresses the algebraic difference between the potentials obtaining at the left and right arm, lead III expresses the differen[illegible] the left le[illegible]

[illegible] electrode from the galvanometer is attached to the limb to be examined, while two of the leads from the central terminal are attached to the other two limbs The third is allowed to hang loose (65) These leads are named aVR, aVL and aVF to distinguish them from the original method in which the central terminal was attached to all three limbs and a second electrode was placed upon the limb to be examined The deflections obtained in this way were small and not easily read By the *augmented* method the deflections are increased by 50% and can be more easily measured It is convenient to refer to these leads as R, L and F as Wilson suggested Modern instruments embody the necessary connections

Œsophageal leads The œsophagus is in relation to the back of the heart, and so might be expected to give valuable information in

the case of posterior infarcts. In practice it has not proved superio to lead F *(66)* In high posterior infarcts which may escape detec tion, the electrode is near the transitional zone between ventricl and auricle, and the fact that Q waves and negative T waves ar normal at auricular levels, makes it difficult to isolate them *(67)*.

Antero-septal infarct. The classical pattern of a transmura antero-septal infarct comprises an rS in VI with a QS or QR i V2 to V3 or 4, and an insignificant Q in the left ventricular surfac leads (V5 and 6, and L) *(57)* (Fig 77).

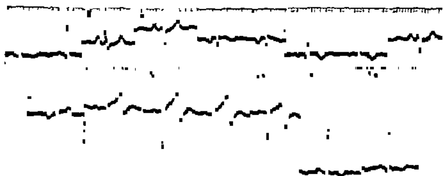


FIG 77. Antero-septal infarct Note small R in V1 with QS in V2 and V3, and QR in V4 Elevation of ST junction and plateau type negativity of T in V3 and 4

In the early stages there may be gross elevation of the RS-T junction from V2 to V4, which usually gives place later to negative T waves Variations of this pattern include a qrS in V1 and 2, with a *QS* or *QR in V3* or *4* *Or there may be only an abnormal decrease* in the voltage of R from V1 to V3. Rather similar appearances may occur in some cases of right ventricular hypertrophy and dilatation RS may be normal in V1 but R may be reduced, or may disappear, in transitional leads to the left, rarely QS waves may be found from V1 to V4 But in right ventricular hypertrophy lead V4R will always have a secondary R without a final S, instead of resembling lead V1, though of lower voltage, and in cases of doubt [illegible] QR complexes in V1 and 2 have also [illegible]

The negative T waves have usually a characteristic shape but it must be remembered that negative T waves may occur also in

pericarditis, and in right ventricular dilatation secondary to a pulmonary embolism Counter-clockwise rotation of the heart may cause a lateral infarct to have the appearance of an antero-septal infarct, but this is not important In fact, using the criteria described, the correlation with the autopsy findings was exact in every case of recent and of healed antero-septal infarction (57)

Antero-lateral infarct. The criteria for this type are well known QS waves, or QR waves, are seen in the left ventricular surface leads —V5 and V6, in lead L and so in lead I. In recent infarcts upward deviation of RS-T junction occurs which later gives place to negative T waves Out of 57 antero-lateral infarcts these changes were found in all but five cases In 27 they were present in V5, V6 and L, in 15 in V5 and in V6 or L, in 8 in V5 only, in 2 in lead L only. The diagnosis was not made in the remainder because the signs were obscured by a left bundle branch block, or because of the presence of a small upstroke in V5 and V6 owing to the displacement of the transitional zone to the anterior axilla, or to preserved islands of intact muscle (70). If the infarct was limited to the subendocardial zone the RS-T junction was usually depressed The diagnostic accuracy is therefore very good.

Lateral infarct. Infarcts occurring principally in the lateral wall are frequently due to occlusion of the circumflex artery They are divided into high and low lateral infarcts

High lateral infarcts show best in lead I,

... may become tall (72) Additional leads taken along the 3rd space in the C3, 4 and 5 positions may show the usual QR or QS waves which are diagnostic

... These features ...



FIG 78. Infarction of lateral wall There is depression of S T interval in leads I and II and deep depression of ST junction in V3 and V4 Auricular premature systoles are present ...

short time only and they resemble those of digitalis saturation; but the Q-T interval is not shortened. Auricular premature systoles may occur in this type, and auricular fibrillation may supervene *(74)*. Subepicardial lateral infarcts have only negative T waves in V5, V6 and lead L and the curves *must then be distinguished from those* of left ventricular hypertrophy.

POST-INFARCTION BLOCK In infarcts involving the free wall of the left ventricle, such as the antero-lateral or lateral infarct, there may be a prolongation of the QRS, and this must be distinguished from a left bundle branch block of septal origin In left bundle branch block the septum is activated from right to left, so that the left ventricular cavity is positive in the early stages. No Q waves can therefore appear in the left ventricular surface leads. In post-infarction block deep and prolonged Q waves are seen in V5 and V6 if the infarct is transmural, or a normal Q may be followed by a notched upstroke of R if the lesion is subepicardial *(75)*.

Posterior infarct. In a transmural infarct the same distinctive features are seen *in lead F, III and to a less extent in lead II* as occur

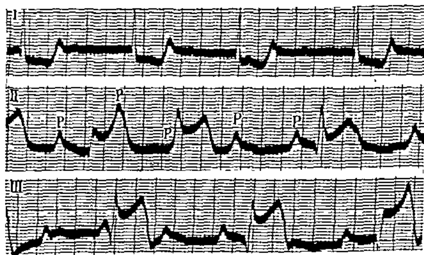


FIG 79. Coronary occlusion with posterior infarction and complete heart block

in the precordial leads, and lead L in anterior infarcts QS or QR waves appear, and in the early stages the RS-T junction is elevated due to the current of injury (Fig 79). Negative T waves in due course take the place of the raised RS-T junction Reciprocal depression

of the RS-T which may be deep, appears in the precordial leads, and to a less degree in leads I and L, if the anterior wall is intact. It is not seen if there has been a previous anterior infarct there.

In the case of small posterior infarcts the position is not so satisfactory for they are liable to be missed more than other types. When the heart is in a vertical or intermediate position few cases escape detection. Only 10 out of 75 cases of posterior infarcts in vertical hearts failed to show characteristic appearances in lead F and these were small infarcts confined to the basal third of the posterior wall. This is because when the heart is vertical lead F faces the posterior wall of the left ventricle and the left side of the septum owing to counter-clockwise rotation. But, when the heart is horizontal, lead F faces more the right side of the septum and posterior wall of the right ventricle, and the curves were normal in as many as 22 out of 35 cases of posterior infarction; in the remainder abnormalities occurred because the infarct extended into the septum *(76)*. It may be possible on occasions to alter the position of the heart from the horizontal by deep breathing or by change of position, and a record with lead F taken on full inspiration or with the patient sitting up, may reveal changes not present in the usual record with the patient lying flat. In another series of 80 cases, posterior infarction was only diagnosed in 47, but in 21 more an anterior infarct, which was also present, was detected. Localised high infarcts accounted for 7 failures, others were due to the presence of left bundle branch block, and incomplete left branch block may have been responsible for some more that were missed. But actually *no* electrocardiogram in the series was reported as normal. Vectorcardiograms were informative in 9 cases in which the electrocardiograms did not help *(77)*.

In the early stages of posterior infarction tall sharply-pointed T waves may be present in V2–V5. The Q waves and negative T waves in III and F then develop later. Tall T waves may occur here [illegible] pain, further [illegible] to 27 mm in [illegible] disappointing. With records taken 7.5 mm below the level of the last intrinsic P wave, no false positives were found, but the infarct was missed in 12%. Lead F was more consistent and in 12% showed abnormal Q waves when the œsophageal lead was normal *(80)*.

Postero-lateral infarct. These infarcts are mainly subendocardial, they were always most dense in that layer and they were confined

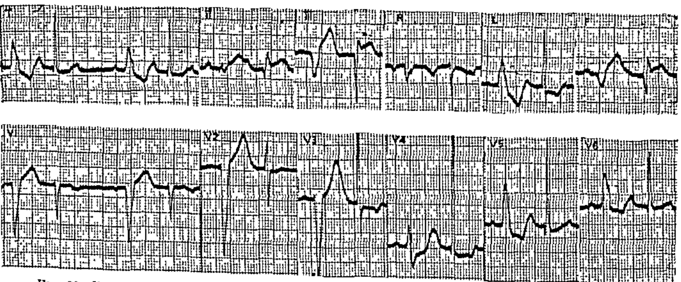


FIG. 80 Recent posterior infarct involving septum. Incomplete A-V heart block with Wenckebach periods L B B B complexes follow normal P-R intervals. Lead F has QR complex and QS with L B B.B. Confirmed at autopsy

to it in 25%. The electrocardiographic signs are those of posterior ... combined with dome-shaped T waves in V5 and V6 and ... was diagnostic in 10, showed ... ior infarct in 12. It failed to ... detect ... type ... leads (82)

Antero-posterior infarct. In 30 cases an anterior infarct involved, in addition, more than the apical third of the posterior wall. In 23 of these there was cardiographic evidence of an anterior and of a posterior infarct In the remainder the posterior infarct did not show owing to a horizontal position of the heart

Owing to the reduction in the opposing potentials elevation of the RS-T junction was seldom seen (83)

Infarction of the right ventricle is exceedingly rare In one such case the cardiogram showed only signs of an antero-posterior infarct (84)

Septal infarct. The septum is frequently involved in an anterior or posterior infarct, and out of 90 such cases the septum was affected

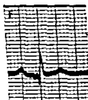
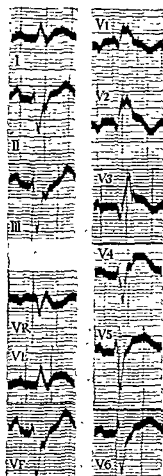


FIG 81 Healed postero-septal infarct Note qrSR[1] in lead F. Coronary occlusion 6 weeks previously. Recent Stokes Adams' seizure

primarily in 6 (85) The development of A-V heart block during the course of infarction is diagnostic (86) (Fig 81) Otherwise the appearances depend upon whether bundle branch block is present or not.

WITH NORMAL CONDUCTION a qrS in V1–V3 is diagnostic if right ventricular hypertrophy can be excluded by the presence of a normal V3R or V4R A similar appearance in lead F suggests a posterior septal infarct (Fig 81) A QS in V1 and V2 also denotes a septal infarct if QR waves are present in leads to the left or if V4R is normal (85) Signs of an acute antero-septal infarct combined with those of posterior infarction are also reliable but rare (86) The absence of the normal Q waves in the left ventricular



and broad Q waves in V1 and V2, and elevated RS-T junction, combined with the prolonged QRS and the delayed intrinsic deflection of a right branch block (Fig 82). Similarly a deep and broad Q wave in lead F associated with a right branch block denotes a posterior infarct involving the septum Bowed and negative T waves also occur.

WITH LEFT BUNDLE BRANCH BLOCK the diagnosis is more difficult, since the delayed activation of the left ventricle causes the cavity to be positive in the early stages and precludes the appearance of Q waves Also some curves with prolonged QRS of left branch block type have QR waves in V5 and V6, and are due to infarcts of the free wall (post-infarction block) A left branch block with Q waves in left ventricular surface leads, and prolongation of QRS to 0 14 sec.

FIG. 82. Anterior infarct with right branch block Note presence of Q wave in V1, V2 and V3, with bowed inversion of T in V1, V2, V3 and V4 The intrinsic deflection is delayed on the right side by 0 14 sec and is early on the left Autopsy confirmation

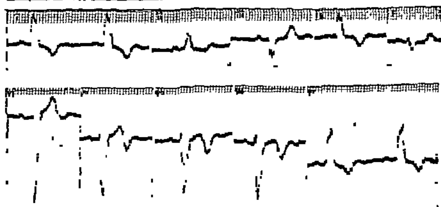


FIG. 83 Left bundle branch block and anterior infarct. Note deeply negative T waves V2-V4

or more, is usually due to complete infarction of the septum, with the negative cavity potentials of the right ventricle passing through to the left side A left branch block with low voltage in the left

with left branch block may be due to an infarct of the lower third of the septum (89) The RS-T displacement and negative T waves of infarction are usually engulfed in the large broad complexes of left branch block, but some curves show them (Figs 83 and 84)

Auricular infarcts. Infarction of the auricles may occur The P waves are dome-shaped or negative and there is also depression of the P-Q interval (90) If there is associated auricular

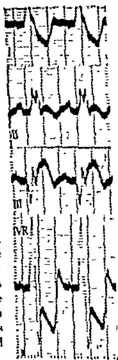


FIG. 84. Posterior infarct with left bundle branch block

son-White syndrome. The Wolff-Parkinson-White syndrome obscures the signs of infarction since Q waves are obliterated by the bundle branch block type of complexes of the anomalous A-V excitation Sharply negative T waves may be present (92), and there may also be deviation of the RS-T (93) The diagnosis is usually made when normal conduction occurs during the course of infarction (94) Normal conduction may be produced by quinidine 0·2 g intravenously, or by atropine 0 9 mg., or by amyl nitrite inhaled three hours after oral quinidine, or even by deep inspiration Digitalis

nodal rhythm, in

in infarction The Q-T interval infarcts and does not

verage was 0 41 sec which is as with digitalis the average

Persistence of electrocardiographic signs. This depends largely upon the size of the infarct. In small subepicardial infarcts with only negative T waves the electrocardiogram has returned to normal in only two days, the average being six months (*98*). In another series negative T waves from V1 to V4 became normal in a few weeks to a year, but some of them may not have been due to infarcts at all (*99*). In transmural infarcts the position is different, and one only was normal when re-examined after a year. It was in fact suggested that a completely normal cardiogram is strong evidence against infarction during the preceding year (*100*), but this does not apply to subepicardial infarcts with only T wave negativity. In some posterior infarcts, where the curve had returned to normal, signs of the old infarct could be made to appear by altering the position of the heart by means of records taken in the sitting or lateral positions (*101*).

In ventricular aneurysm the electrocardiographic changes may become fixed. One such patient had a transmural anterior infarct in 1938 and the curve has altered little during the intervening twenty years. He has developed a moderate ventricular aneurysm but has never been off work.

Effect of pericarditis. Acute diffuse pericarditis causes elevation of the RS-T junction in all leads. Later, T becomes negative. Since the injury is limited to the subepicardial zone Q waves are not found. The upward displacement of the RS-T may efface the RS-T displacement of a posterior infarct in the chest leads, or of an anterior infarct in leads F and III. Diffuse pericarditis should be borne in mind when the electrocardiogram alters during the first few days after infarction, and the possibility of an extension of the infarct is being considered. Localised pericarditis over an infarct does not effect the electrocardiographic signs due to the infarct.

Accuracy of the electrocardiographic diagnosis. The diagnosis of cardiac infarction by means of the 12 lead electrocardiogram is among the most precise in medicine. If a patient has symptoms it is very rare indeed for the electrocardiogram to mislead. Abnormal features may take a day or two to develop, but, if serial records remain normal, some other cause for the pain must be sought. Difficulties may arise in two circumstances. First in the case of multiple infarcts one of them may be missed, but this is not important. Secondly high posterior and high lateral infarcts are less accessible than infarcts in other positions. The normal chest leads do not show them, and lead F is unreliable when the heart is horizontal. It is sometimes possible to record signs of infarction by means

of chest leads taken in the third space if the usual ones are normal and L shows a negative T. In the case of posterior infarcts, one can take lead F in full inspiration, which makes the heart more vertical Small localised subendocardial infarcts in these positions may nevertheless escape detection. This mainly happens when the infarction has caused no symptoms, having occurred during the course of congestive failure, and the record is taken when the infarct is healed

Cardioscopy. Since the patient has to stand for these procedures, cardioscopy should not be employed in recent infarction Pulsation at the apex, or just above it, may be reversed with a localised outward expansion during systole A double pulsation or delayed pulsation may also be seen The antero posterior position is used for anterior infarcts, and also furnishes information about some posterior infarcts Half-way towards the right anterior oblique position is also helpful for the detection of ventricular aneurysms which in that position protrude beyond the left border of the heart. Pulsation may be absent or diminished in the area involved, but diminished pulsation is also found in cardiac failure with gross enlargement of the heart, constrictive pericarditis and in pericardial effusion whilst local

may be gone by the end of a year If they persist, a permanent thinning of the ventricular wall is present, and a cardiac aneurysm may develop

Kymograms allow the pulsations to be recorded by means of a multiple slit grid, and are measured on a film Abnormal kymograms can be recorded in most cases of infarction, and the site of abnormal pulsation agrees well with the electrocardiogram

Differential Diagnosis

It should be emphasised that none of the

almost always establishes the diagnosis, unless there are two causes present

ACUTE ABDOMINAL DISEASE. Pain in the epigastrium may resemble that of a perforated peptic ulcer, gall stone colic or acute pancreatitis Infarction may follow a severe hæmatemesis, it is

rare for an infarct and an acute ulcer, or acute cholecystitis, to develop simultaneously.

Hiatus hernia. The pain caused by nipping of the portion of the stomach which has herniated into the chest may on occasion *closely simulate an infarct. It may be substernal and may occur* at night (*102*) Patients who have a hiatus hernia and have had a cardiac infarct find it difficult to distinguish the two types of pain Relief may, however, come suddenly as the hernia slips back, and is assisted by sitting up. A barium meal in the Trendelenburg position will show the hernia

In the absence of an electrocardiogram, the following points will suggest infarction

1. A history of previous attacks of substernal pain on exertion
2. The presence of dyspnœa, without the pain of pleurisy
3. *Evidence of pericarditis, or of pulmonary congestion.*
4. The pain almost always tends to spread upwards.
5. Absence of epigastric tenderness, and of the abdominal rigidity of peritonitis.

PNEUMOTHORAX OR PNEUMOMEDIASTINUM cause pain, dyspnœa *and shock* In pneumomediastinum the pain may be *substernal.* A small left-sided pneumothorax can cause pain in the left upper chest which may persist for days A systolic click may be found, which the patient can hear himself In mediastinal emphysema peculiar crackling sounds like those of surgical emphysema—they change with the heart-beat and breathing—are audible over the precordium All these conditions tend to occur in younger age groups than infarction

DISSECTING ANEURYSM Although most cases of dissecting aneurysm, if they survive, develop distinctive signs, in the early stages the diagnosis may be very difficult if the coronary blood flow is affected, as the electrocardiogram will show evidence of *ischæmia* This may occur where the dissection occludes the mouths of one or other of the coronaries or where they are compressed either by extravasated blood or by a hæmopericardium (*103*)

An œsophageal pouch may give rise to substernal pain through the effect of distension of the œsophagus, and the pain may last an hour or more.

Complications. About three-quarters of the patients, if kept in bed, will make a straightforward recovery Of the complications that occur in the remainder, most may be expected during the first *fortnight.*

Death may take place from *ventricular-fibrillation*, or from a reflex coronary spasm while pain is still present

complication as might be
t ventricle.
nosed, and

sinks into coma.

Hypostatic pneumonia may be the consequence of severe pulmonary congestion aided by the immobility of the patient The
in respiratory rate, tachycardia,

previous infarcts, or whose hearts are enlarged from hypertension

RUPTURE OF VENTRICLE During the first few days recurrent attacks of angina at rest accompanied by pulmonary congestion
of the ventricular wall, and death *may occur*
We have seen it within
herwise it is more likely
As a *rule death is almost*
tamponade to develop, with signs of venous engorgement, cyanosis and respiratory embarrassment, which soon proves fatal (*105*)

PERFORATION OF THE INTERVENTRICULAR SEPTUM Rupture of the septum usually takes place near the apex, and more often to the front The perforation can vary from the size of a probe to 4 cm in length (*106*) The septum may be massively necrosed, the electrocardiogram showing evidence of septal infarction Another factor is cardiac enlargement due to previous hypertension or old age The rupture causes precordial pain and shock which may come within fourteen hours of infarction, but usually occur from the 3rd to the 12th day (*107*) The harsh systolic murmur of a ventricular septal defect, usually accompanied by a thrill, is heard to the left of the sternum Intractable failure of the right ventricle then results owing to the left to right shunt One patient who was catheterised had a pulmonary pressure of 75 mm (*106*) Most cases die soon after perforation but one survived 6¼ years with persistent right ventricular failure and œdema (*108*) Another died from a second infarct (*109*) If an aneurysm of the septum forms first, the signs of subsequent rupture are less conspicuous, and the development of a systolic murmur may be the only clue (*110*)

Rupture of a papillary muscle has occurred in posterior infarction (*111*) and in lateral infarcts due to occlusion of the circumflex

branch (*112*). A loud systolic murmur develops at the apex and there may be a thrill. This complication is fatal.

Arrhythmias. *Auricular fibrillation* is uncommon. Paroxysms usually begin during the first week. Lateral infarcts have a tendency to be accompanied by fibrillation, or the auricles may be involved in the infarction. In some severe attacks, fibrillation commencing near the onset increases the gravity of the prognosis. In others, who may have suffered from paroxysms before, or have a mild form of rheumatic heart disease, the paroxysms are of little importance and do not last long. Auricular flutter and paroxysmal auricular tachycardia are rare. Out of 5 cases of auricular tachycardia 3 followed the administration of large doses of digitalis (*113*).

Ventricular tachycardia is a serious complication which is likely to prove fatal unless it responds to prompt and effective treatment The appearance of numerous *ventricular premature systoles* particularly when these arise from several foci, may be a precursor of ventricular tachycardia.

A-V heart block signifies a septal infarct or an extension to involve the septum. Posterior infarction is usually present, and complete heart block comes on from the first to the fifth day (Fig. 79). The prognosis is usually bad the patient may develop Stokes-Adams' attacks, or collapse owing to the greatly diminished cardiac output due to the combination of the slow rate and low blood pressure; but sometimes the block clears up.

Thrombo-embolism. The prevalence of thrombo-embolism has been much disputed as there are divergent views as to what constitutes a thrombo-embolic incident. Some would include all extensions of the original cardiac infarct, and any emboli however small, that may be found at necropsy. Others would restrict the use of the term to episodes which can be ascribed clinically to an embolism. Mural thrombi are common Most of them are found near the apex of the left ventricle but a few are in the right ventricle, through an extension of the infarct through the septum, and also in each auricular appendage The left ventricular thrombi are most frequent in large anterior infarcts, especially if congestive failure has been present They may be due to incomplete emptying of the ventricle in the area of a large infarct (*114*) But they rarely become detached and, when they do, they often lodge in some organ such as the kidney or spleen, where they do little harm Out of 84 systemic emboli only 9 caused death; five in the brain and two each in the femoral and mesenteric arteries (*115*). An unexplained hemiplegia may be due to cerebral embolism from a cardiac infarct

But hemiplegia, convulsions and coma may also occur in patients with advanced cerebral arteriosclerosis in the absence of emboli, and are due to the impairment of the cerebral circulation consequent upon the diminished cardiac output. There may be a primary cerebral thrombosis from the same reason Patients with cerebral emboli from intraventricular thrombosis often do surprisingly well and recover without any residual palsy Embolism of a peripheral artery following coronary occlusion may be a disaster The patient is



FIG 85 Aneurysm of the left ventricle

not in a condition to stand embolectomy and one can only try to re-establish the circulation with intravenous papaverine and heparin

Pulmonary emboli arise chiefly from venous thrombosis in the calves, local thromboses causing infarcts in different organs are also common Both these complications are favoured by the immobility of the patient

CARDIAC ANEURYSM If an infarct has involved the whole thickness of the ventricular wall, local weakening may lead to the formation of a cardiac aneurysm They seem to occur especially in those who rested a few days only during the acute phase [illegible]

actual apex thrust. On X-ray examination the left border of the heart assumes a somewhat rectangular appearance. A localised bulge may be found on the left border (Fig 85) and calcification may be visible within it (*117*) In the right oblique position the aneurysm may project as a flat ledge towards the back of the sternum (Fig. 86). The sac may show expansile pulsations, or none at all The prognosis is fair and considerable activity is possible Patients



FIG 86 Aneurysm of the left ventricle Oblique view of case shown in Fig 85.

usually die from congestive failure, or from repeated emboli due to thrombosis in the sac Rupture is very rare

Left shoulder pain A curious condition of pain, with limitation of movement at the shoulder may develop in the months following infarction The disability simulates a subacromial bursitis, and there is usually a history of some pre-existing shoulder lesion The pain can be reproduced by lifting the arm above the head (*118*) Relief can usually be obtained by heat and massage

Treatment

. . . . . of the heart

MORPHIA Morphia should be given at once if there is pain or severe dyspnœa, for the sooner the pain is controlled, the less likely is the patient to die from syncope. Intravenous injection gives most rapid relief and is safe Morphia, 1/6 grain given intravenously, and 1/4 grain subcutaneously with atropine sulphate 1/100 grain should be given followed by further 1/4 grain doses subcutaneously, as required.

REST IN BED The patient should be put to bed at once. In severe attacks this is obviously needed but minor attacks may be missed These patients are more likely to develop post-infarction angina or cardiac aneurysm He must not put his foot to the ground but can be helped on to a commode for actions of the bowels For elderly people this is less of an effort than straining on a bed pan. The modern [illegible] time th [illegible] recomm [illegible] [illegible] keeping with current surgical practice, and lessens the risk of venous thrombosis in the calves If pulmonary congestion has developed, or the pulse rate has exceeded 100, or a gallop has been present, or fever has been high, rest in bed up to five weeks will be needed.

OXYGEN Oxygen therapy is valuable if cyanosis develops at any stage, and also if pain persists or recurs, in spite of adequate doses of morphia at the onset A B L B mask or spectacles should be used, or an oxygen tent.

Coronary dilators Experimentally it has been shown that cardophylin or atropine given promptly reduces the mortality rate in dogs by one-half [illegible] intravenously [illegible] found it both s[illegible] in 2 ml intrav[illegible] cases providing the injection is made slowly

Pressor amines Attempts have been made to revive patients with circulatory collapse and systolic pressures in the region of 80 mm Hg by means of a noradrenaline drip at the rate of 1 mg per minute or by giving 5–20 mg intravenously at frequent intervals, with the aim of keeping the systolic pressures at about 100 mm (*122*) It was supposed that noradrenaline did not share with adrenaline the tendency to cause ventricular arrhythmias This

is not true. In animals noradrenaline produced ventricular tachycardia and A-V dissociation. 22 patients suffering from shock following infarctions were given a noradrenaline drip and electrocardiograms showed multifocal ventricular premature systoles and *ventricular tachycardia; none survived (123). Mephine is valuable* for a short time, 15 mg. of the sulphate intramuscularly.

DIGITALIS. The great majority of patients with cardiac infarction do not require digitalis, which should be reserved for those who develop pulmonary or systemic congestion. It is the only form of treatment that may avail when severe shock is accompanied by pulmonary congestion. Other indications are evidence that the heart is enlarging, and the presence or development of auricular fibrillation or a gallop rhythm If care be taken to avoid overdosage, digitalis does not cause ventricular tachycardia, or other arrhythmias, as was formerly thought (*119*). It is advisable to give the *loading dose in the form of intravenous digoxin 1 0 mg* or Cedilanid 1·2 mg, and to follow either with intramuscular cedilanid, 0 4 mg. daily, or with digitalis folia, 3 grains daily (*124*) Thus any cumulative effect is avoided

QUINIDINE OR PROCAINE AMIDE should be given at once intravenously to abolish the dangerous complication of ventricular tachycardia (see p 339) Quinidine is best given as the dihydrochloride, and preferably under electrocardiographic control so that the injection can be stopped as soon as normal rhythm returns 0·6–0 9 g. may be needed The intravenous dose of procaine amide is 0·5–1 g (*125*).

DIET. In severe cases, or when vomiting is present, only drinks sweetened with glucose to combat acidosis should be given for some days Full doses of atropine may control vomiting During this time the bowels should be left alone If a natural action has not taken place, an enema or suppository can be given later During the rest of the period in bed, small helpings should be the rule otherwise the tendency will be to put on weight

Anticoagulant therapy. The use of anticoagulants in cardiac infarction has been the subject of much controversy Some give them in all cases, others do not use them at all, while some employ them only in cases where they think the infarct is transmural, or where there are special indications

Those who use them in all cases believe that in severe cases the risk of thrombo-embolism is materially lessened, while mild cases may be prevented from becoming severe through further coronary thrombosis. In one series the mortality was halved with anti-

coagulants Pulmonary infarcts were greatly reduced, though the number of peripheral arterial emboli and of ventricular thrombi were unaltered (*126*) In another series the mortality fell from 28% to 12%, thrombo-embolism from 38% to 7% (*127*) In another, where the total mortality fell by 11%, the greatest reduction occurred in those over 60 years, in those with congestive failure and in cases of diabetes (*128*) Moreover it has been claimed that the course of infarction is in some way influenced favourably by anticoagulants and that patients do better if they are taking them (*129*) This may possibly be due to earlier recanalisation of the occluded artery The femoral arteries of rats occluded experimentally, recanalised in a month when they were given tromexan, whereas in the controls

occasionally fatal They prefer not to use a remedy which itself can be dangerous In a series of 150 cases, selected with care so that the controls were of the same age and sex as those treated, the mortality in each group was 30% (*131*) In such an unpredictable disease as cardiac infarction the method of the alternative case has obvious fallacies

The middle course is to restrict the use of anticoagulants to severe cases of transmural infarction in which intraventricular thrombi are likely to be present, and to include those who have had a previous infarct, those suffering from varicose veins and those who are obese (*132*) The risk of emboli in subepicardial infarcts is only 0 8% and the mortality 3%, which is not sufficient to warrant anticoagulant therapy

Selection of cases Cases may be selected for anticoagulant therapy by means of the heparin retarded coagulation time (*133*) 0 1 ml of normal saline containing 0 004 mg. of heparin is placed in a tube with a bore of 7 cm The blood to be tested is added to a level of 1 1 ml and the tube is gently inverted several times

... a series of cases of infarction where the time remained normal, no patient died In those with accelerated coagulation the mortality in the first attack was halved by anticoagulants (*134*)

ACTION OF ANTICOAGULANTS *Heparin* increases the clotting time but the precise mode of action is unknown It may inhibit the thrombin fibrinogen reaction which produces fibrin

Coumarin derivatives. These act indirectly, and so slowly, through the liver. They probably inhibit the formation of prothrombin. They are similar in structure but antagonistic to menadione bisulphate (Vitamin K). The coumarin drugs are also thought to act on *Factor VII (135)*, which together with the Christmas Factor and antihæmophilia globulin, is needed to complete the formation of thrombin.

QUICK TEST (*136*) *The prothrombin time* is the time that a preparation of thrombokinase (thromboplastic substance) takes to coagulate the plasma of the patient. The thrombokinase is usually obtained from extracts of brain. The normal time varies from 12 to 17 sec. and each batch of brain extract is standardised against the blood of a normal subject. The *prothrombin index* expresses the result as a percentage of this normal value Thus if the normal time obtained with the thrombokinase used was 17 sec., and the time for the patient was 34 sec., the index would be 50% If, however, the normal for the batch of brain extract was 12 sec, a prolongation to 34 sec. would equal an index of 35%. The *prothrombin concentration* is calculated from the prothrombin time by means of a graph, and endeavours to express the actual amount of prothrombin present as a percentage of the normal In this country the *prothrombin time* is most commonly used, although the prothrombin index gives the most accurate information.

The aim of treatment is to decrease the prothrombin index to between 30 and 50%. This corresponds to prothrombin times of *30–50 sec. At this level it is claimed that no fresh thrombi will* form, nor will accretions be added to existing thrombi; it is the fresh clots which are friable and liable to become detached.

DICOUMAROL is the original anticoagulant, isolated at first from sweet clover and later synthesised It is supplied in 50 mg. tablets. Dicoumarol takes from 48 to 96 hours to come into action 300 mg is given on the first day and 200 mg on the second. Subsequent doses are controlled by the prothrombin times

Ethyl biscoumacetate (Tromexan) has a time lag of 24–36 hours, which is the shortest of any of the coumarin derivatives It is supplied in 200 mg. tablets. The loading dose is 1600 mg followed by about 800 mg. in two doses

PHENYLINDANDIONE (DINDEVAN) Although dindevan has a different structure from the coumarin drugs, the action is very similar The time lag is 24–48 hours. Dindevan has largely superseded dicoumarol and is the most commonly used anticoagulant. It is supplied in 50 mg. tablets. *200 mg. are given at once followed by 100 mg.*

in 12 hours (*137*). Maintenance doses of about 75 mg are given twice daily (*138*), but the actual dose is controlled by the prothrombin test. If the renal function is depressed smaller doses will be required as excretion is diminished (*139*). An alkaline urine may turn to an orange-pink colour with dindevan (*137*).

[illegible]

Administration The aim of treatment is to keep the prothrombin index between 30 and 50%, which corresponds to a prothrombin time of 30–50 sec. This is not always easy to attain because there are spontaneous variations in the coagulability of the blood following infarction. It has indeed been suggested that a state of hypercoagulability causes the thrombosis. After two days an anticoagulant substance is liberated from the necrotic muscle which becomes exhausted in about eight days. Then hypercoagulability is resumed (*140*). Treatment is continued until the risk of emboli is over, usually when the patient is allowed up. On account of the [illegible]

[illegible] This is followed by 15 mg every six hours.

Contra-indications. Anticoagulants should not be given to patients with gastric ulcers owing to the risk of bleeding, nor to those with blood diseases associated with purpura. Patients with advanced hypertension, frequency of micturition, and recent prostatectomy are also unsuitable. Care must be taken in those with congestion of the liver and other conditions such as cachexia, in which the liver functions are depressed.

Toxic reactions. In overdosage there may be bleeding into the skin, from the intestine, *or kidneys*, or into the brain. The incidence of bleeding varies *greatly* in different series. In one it occurred in 20% but consisted mainly of hæmaturia detected by the benzidine test. (Bleeding was less frequent with [illegible]

[illegible]

[illegible] to the coumarin drugs is menadione bisulphate 5–20 mg given intravenously, or Vitamin K_1 tablets. In an emergency 500 ml of blood will restore the blood prothrombin

to normal for eight hours The antidote for heparin is protamine *sulphate 50–100 mg. given intravenously (127)*

Long-term treatment. Anticoagulant therapy can be continued for years in the hope of avoiding recurrences of infarction The prothrombin time is estimated first at weekly and then monthly intervals, the index being kept at about 50%. The treatment is justified when a patient has had two or three infarcts in rapid succession In one series observed up to six years the rate of recurrence fell from 27 to 8% (*141*). Dicoumarol is a good anticoagulant for long-term therapy (*119*). Many prefer dindevan.

Summary. Assessing the value of any form of treatment in cardiac infarction is difficult because the course of the disease is entirely unpredictable. Comparison with controls is therefore unreliable. In one series the conclusion was reached that anticoagulants were of doubtful value. It is our practice to give them to all patients whose infarcts we judge to be large and transmural. It does not seem justifiable to use an inherently dangerous remedy *in subepicardial infarcts in which the prognosis is almost uniformly* good The small risk of an extension of the infarct must be balanced against the risk of a hæmorrhage resulting directly from the treatment. It is necessary also to transfer the patient to hospital, or to arrange for prothrombin estimations to be done, every three or four days, some prefer every other day

With respect to the choice of anticoagulants, dindevan is generally preferred, but one of us (C.W.C.B) has used dicoumarol almost exclusively for twelve years It was found to be more difficult to control the prothrombin level with tromexan Dindevan was good as, but no better than, dicoumarol. The drug has occasionally been stopped on account of petechiæ or hæmaturia but no major hæmorrhage has occurred, nor have there been any peripheral emboli. There appears to be little difference in action or toxicity between the different compounds available and it is probably better to learn how to control one and to keep to it (*119*).

After Care

A prolonged convalescence is necessary after infarction in order to allow healing to proceed satisfactorily, and the rest of the myocardium to adjust itself to maintaining the circulation Even with a small infarct and without complications, the patient should wait three months before resuming his work *Large infarcts require* longer. A further slow improvement may then be expected which will continue until a year has elapsed

Prognosis

In a follow-up of 200 patients seen 25 years previously it was [illegible]

the absence of cardiac enlargement due to hypertension, or diffuse coronary artery disease. The risk of successive attacks cannot be assessed, but they are common, and the patient may survive three or four, dying finally in congestive failure.

ANGINA PECTORIS

Herberden, in 1768, first described a "disorder of the heart, marked with strong and peculiar symptoms, considerable for the kind of danger belonging to it" Parry wrote in 1799, following a suggestion of Jenner "The rigidity of the coronary arteries may act, proportionably to the extent of the ossification, as a mechanical impediment to the free motion of the heart, and though a quantity of blood may circulate through these arteries . . . yet there may probably be less than what is requisite for ready and vigorous action." Recent work has done much to prove the truth of these older observations Herberden's angina is due to a transient relative *anoxæmia* of the myocardium, and all attacks are attended by a possibility of sudden death

Diagnosis

The [illegible] of the pain the mode of the onset the type of the pain its duration

Site of pain The pain is substernal Often it is described as being [illegible] ver the heart, but questioning will elicit the fact that it spreads [illegible] the mid-line Occasionally it is felt chiefly at some other point, such as the *jaw* Cases have been known where it was confined to one or both *arms* If severe, the pain radiates over the upper chest and down the *ulnar* side of the left arm, in the area supplied by the first two left *dorsal roots* Tingling or numbness are also felt at the elbow or wrist Sometimes there is a spread to the right side over the corresponding areas In congenital dextrocardia, the pain has been noted on the right side

Mode of onset. The pain is brought on by exertion or emotion. As with dyspnœa, it is first noticed while walking up hills, later on the level Attacks come on more easily in cold or windy weather They are especially liable to occur if exertion is undertaken soon after a meal, as the process of digestion itself entails an increase in the output of the heart. Patients often attribute their pain to indigestion. Although the onset is abrupt, the pain increases in intensity and very soon becomes intolerable if the exertion is not stopped The pain always makes the patient stop or slow up

Type of pain. The pain is usually described as a "tightness" or "pressure", as if there was something inside which was too big for the chest to hold. It may develop into a sense of intense constriction In many attacks, however, a dull ache only is felt, and occasionally a burning sensation is experienced The pain is never stabbing in character, but is continuous until the exertion ceases Sometimes dyspnœa accompanies the pain and the patient may be uncertain as to which makes him stop. Especially when emotion is a factor the patient may refrain from all movement, and even respiration may be restricted. This contrasts with the restlessness of many patients with infarction. In cases associated with emotion there may also be a sense of impending dissolution, and sweating and pallor may be conspicuous These features are probably due to the secretion of adrenaline.

Duration In angina of effort the pain does not usually last more than a few minutes, and passes off quickly as the exertion ceases. If the attack lasts longer than fifteen minutes the possibility of infarction should be considered On the other hand, a pain in the chest lasting less than a minute is not due to angina pectoris Sometimes a patient is able to continue his exertion and walk off his pain. This first effort angina may be due to spasm (*144*) or lack of dilatation of the arteries

Ætiology

ISCHÆMIC HEART DISEASE The most common cause of angina is ischæmia of the heart muscle due to disease of the coronary vessels Infarcts are frequently found in patients who have had only angina of effort. This seems to happen more often when the infarct has not been due to coronary occlusion (*53*) On the other hand angina may begin after a coronary occlusion, particularly if the patient has not been kept at rest

SYPHILITIC AORTITIS Rarely proliferation of the intima round the mouths of the coronary arteries may occlude them almost

completely This happened in 7 out of 220 cases of aortitis (*145*). Multiple small areas of myocardial fibrosis were found.

CALCIFIED AORTIC STENOSIS leads to a gross hypertrophy of the left ventricle In grossly hypertrophied hearts the new capillary formation may not keep pace with the hypertrophy of the muscle fibres, so that the cells are poorly nourished Their increase in diameter makes the diffusion of oxygen through their substance difficult The rigidity of the valves interferes with the filling of the coronary circulation, in addition the systolic pressure is low. Angina is common in old men with aortic stenosis.

Mitral stenosis. Angina is very rare in mitral stenosis and in any case is difficult to distinguish from rheumatic chest pain Cases have been reported when the pain disappeared after a successful valvotomy It was suggested that the low cardiac output due to the obstruction lead to angina owing to the small flow of blood through the coronary circulation (*146*)

Congenital heart disease A few cases have been met in severe pulmonary stenosis and in pulmonary hypertension when there was no right to left shunt (*147*) Here there was an obstruction in the pulmonary circuit leading to a small fixed output The pain of pulmonary hypertension is not relieved by nitrites but may respond to cardophylin (*148*).

Rheumatic aortic incompetence Occasionally in young people with free aortic regurgitation of rheumatic origin attacks of cardiac pain occur at rest The attacks are caused by emotion in individuals with unstable vasometer systems The blood pressure rises considerably during the attack, and the heart rate increases. The tachycardia is probably of more importance in producing pain than the rise in pressure Amyl nitrite gives quick relief Pressure on the carotid sinus relieves the pain by instituting a depressor mechanism

Anæmia When the hæmoglobin value falls below 50% cardiac pain on exertion may occur Myocardial anoxæmia through the diminished power of the blood to carry oxygen is the cause. If coronary artery disease is present too, pain will be felt with a lesser degree of anæmia

Hypoglycæmia It was formerly thought that an overdose of insulin would cause angina However, when patients with angina had their blood sugar levels reduced to 38 mg. per cent with intravenous insulin none got angina, although they had other symptoms of hypoglycæmia (*149*)

Tachycardia A rapid rate such as occurs in prolonged attacks of paroxysmal tachycardia, may occasionally give rise to angina.

The diminished output leads to insufficient filling of the coronary vessels. Angina pectoris may occur in thyrotoxicosis (*150*) (p. 227). Exophthalmos may be absent and the thyroid may not be enlarged; but the hair may be prematurely grey and transient glycosuria or paroxysmal auricular fibrillation may be present. Angina pectoris is not found in association with established auricular fibrillation.

Spasm. Attacks with electrocardiographic changes have been recorded in subjects who are sensitive to tobacco after smoking a cigarette. These attacks are probably due to spasm of the coronary arteries. Spasm has been seen to occur frequently in the cerebral arterioles of rats made hypertensive by renal ischæmia (p. 181), and may involve the coronary arterioles more frequently than is supposed.

The blood cholesterol is frequently raised in angina. Many patients with hereditary xanthomatosis, which is due to hypercholesterolæmia, suffer from angina. The bearing of cholesterol on coronary disease is discussed on p. 238.

Electrocardiograms. Electrocardiograms often show evidence of an infarct. The presence of myocardial disease may also be shown by a bundle branch block or heart block, by a low voltage curve or by notching of the QRS. In fact, any abnormality affecting the ventricular complex supports the diagnosis of angina pectoris.

EXERCISE TEST. *If the electrocardiogram is normal an exercise* test can be performed. The "two-step" exercise devised by Master (*151*) is suitable, in which the patient walks up two steps and down two steps on the other side. He then turns and repeats the process. [illegible] is felt

before the exercise, as the test is dangerous in the presence of recent infarction. Otherwise it is safe.

Curves of ischæmia. Usually the RS-T junction becomes depressed in the left ventricular surface leads and this is seen best in V4 or V5. The depression is probably due to a current of injury arising in the subendocardial zone, which is especially vulnerable on account of the poor blood supply. A drop of more than 2 mm. is diagnostic. Less often T becomes negative in these leads, or in leads L or F, or the RS-T may become elevated in lead F. If there is much tachycardia and the P waves are prominent, the auricular T waves may depress the RS-T segment and simulate ischæmia (*152*). More pronounced changes have been found on rare occasions in which records have been taken during attacks of spontaneous angina. In

one there was such marked elevation of the RS-T junction that R and T became fused. The curve was normal in 8 minutes. It was thought that the attack was due to coronary spasm (*153*). In another Q waves with elevated RS-T junction developed from V1 to V4 during an attack of angina and disappeared in a few minutes (*154*).

Anoxæmic test The patient breathes an atmosphere of 10% of oxygen and 90% of nitrogen for twenty minutes unless the pain comes on earlier Pure oxygen is then substituted (*155*). The criteria for an abnormal response is the same as for the exercise test Positive results were obtained in 50% (*156*). The test is probably an index of the coronary reserve (*157*) Unpleasant reactions from the anoxæmia, such as convulsions, mental confusion or pulmonary œdema, have occurred in a proportion of patients so that the test does not appear to be suitable for clinical use The Q-T interval has been measured during the anoxæmic test The Q-T interval is longer than normal in angina and increases still more during anoxæmia Positive results were obtained in 90% (*158*)

ANGINA AT REST Apart from the attacks brought on by emotion, induced by smoking, or caused by conditions associated with extreme tachycardia, anginal attacks may commence during sleep. They are found fairly frequently in association with syphilitic aortic reflux Patients who suffer from these attacks have reached the stage when such minor causes as a bad dream, or overloading of the stomach, or even slipping into an uncomfortable position during sleep, may be sufficient to precipitate an attack The prognosis is bad, and death is imminent In some cases the adoption of a recumbent position will cause pain almost at once (*angina of decubitus*)

Differential Diagnosis

CERVICAL SPONDYLOSIS A prolapsed disc in the neck or upper dorsal region may mimic angina closely. The pain, though it starts in the back, spreads round across the chest and down the arms. It is frequently brought on by exertion such as [illegible]

[illegible] of rheumatism, such as pain in the shoulders The [illegible]

[illegible] xercise,

[illegible] superficial

[illegible] over the trunk. *Left submammary pain* is a common complaint in women It consists of a persistent dull ache

which is often worse on exertion or emotion. The apical region is tender to pressure, and palpation of the tender area reproduces the pain about which complaint is made. Nearly every patient is exact about this, which makes the differential diagnosis easy Fibrositis may involve the intercostal muscles round the sternochondral junctions in the second, third and fourth left spaces This may lead to precordial pain on exertion or emotion, due to the fuller movements of the chest accompanying increased respiration When the fibrositis affects the pectoralis minor, the pain is in the upper chest and is referred down the left arm. But again palpation of the tender spots will reproduce the pain, and the statement of the patient can be relied upon. If he has angina, he will say that his real pain is different. Both these conditions are also found in the right side though less often, but the patient does not associate the pain from them with his heart.

GASTRIC AND ŒSOPHAGEAL PAIN. Stabbing pains in the region of the apex occur frequently They probably arise in the stomach, or diaphragm and are of no significance as regards the heart.

Burning pain arising from the stomach, or reflexly from the gall-bladder, may suggest angina, if the pain occurs some time after food, and the patient associates it with exertion Disease of the gall-bladder and angina may co-exist, and the patient may suffer from both types of pain The symptoms are then very hard to disentangle, but anginal pain is felt across the chest while œsophageal pain which is burning in character tends to pass up from the epigastrium to the throat in the mid-line. Also the gall-bladder will be tender. Pain arising from a hiatus hernia is not associated with exertion, and lasts longer than effort angina. The pain is linked with food and posture and œsophageal symptoms.

Treatment

GLYCERYL TRINITRATE is the most satisfactory drug to stop the attack Tablets of 1:100 or 1:130 of a grain when chewed and dissolved in the mouth act in two or three minutes The effect lasts about fifteen minutes, and intelligent patients can use the drug to prevent attacks by taking a tablet shortly before the moment at which experience has taught them to expect pain The drug is not cumulative, and as many tablets as are needed can be taken each day. Octyl nitrite is supplied in tubes and is mild and easy to use. Amyl nitrite, the most potent vasodilator of all, is of some value in attacks associated with a rise in blood pressure, it is apt to be disturbing, both to patient and others.

AVOIDANCE OF ATTACKS. The patient should be instructed as to the nature of his attacks, and warned not to attempt exertion soon after meals. Meals should be taken dry, and the stomach must not be overloaded at any time. A reduction in weight, in those who are obese, will result in an increased effort tolerance. Especial care should be taken in cold weather: a hot drink can be taken before going out. An abdominal belt may help. Smoking should be allowed only after meals. Many patients find they are better without it altogether, and give it up Alcohol in moderation does no harm; whisky is often beneficial.

METHYL THIOURACIL. Thiouracil lowers metabolism and it lessens the work of the heart 0 2 g given twice daily will always diminish the frequency of attacks after about a fortnight. Maintenance doses of about 0 2 g daily can then be substituted But thiouracil has [illegible] de myxœdematous. They feel [illegible] Thiouracil should be reserved [illegible] sible to control attacks with trinitrin, it is not advisable to give it to anyone engaged in active work Thiouracil has also certain dangers *There is a small risk* of agranulocytosis and one patient who had become free of all pain died suddenly and was found to have pericardial and bilateral pleural effusions as the result of the myxœdema.

Pentærythol tetranitrate (*peritrate*) This long acting nitrite is often effective In one series 70 mg daily reduced the number of trinitrate tablets required to one-tenth (*159*) Peritrate given 6 hours previously modified the electrocardiogram *favourably* after the exercise test (*160*) We have found the drug unreliable Many patients are improved but in others it has no effect

Quinidine sulphate 5 grains four times daily *reduces* the frequency *of attacks* [illegible] bee [illegible] ([illegible] ally [illegible] (*162*), Khellin (*163*), Ethaverine, a papaverine compound (*164*), are useless In anxious patients phenobarbitone helps considerably

Surgical measures. Enterprising surgeons [illegible]

[illegible] adhesive pe [illegible] results were [illegible] during the operation The post-operative electrocardiogram showed evidence of pericarditis for

some months (*165*). The sensory tracts leading from the heart pass through the upper four thoracic sympathetic ganglia. These can be either injected with alcohol or resected, or the posterior sensory roots can be cut as well (*166*). Alcohol injections gave complete relief on the side of denervation in 60%, while resection gave relief in 76%. The sensory roots were cut in only a few cases of severe angina of decubitus Surgical procedures of this kind have not found much favour in this country.

Prognosis

The prognosis is very variable. There is always a risk of infarction, and sudden death from syncope or ventricular fibrillation may occur in any severe attack. The course is slowly progressive as a rule. Attacks of angina pectoris may clear up if the patient subsequently has an occlusion, and attacks which arise following an occlusion may cease after a time. The average expectation of life is over nine years, and some lived more than twenty years (*167*) The average age at death was 65 years As a general rule the frequency of the attacks and the amount of effort required to produce them are good guides to prognosis. Nocturnal attacks occurring regularly have the worst prognosis.

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escape if the auricular impulse is delayed, as on forced expiration which raises the vagal tone (Figs. 89 and 90). In sinus arrhythmia alteration in the shape of the P wave is often seen in expiration,



FIG 88 Nodal Rhythm Note inverted P waves (P_1) following the ventricular deflections.

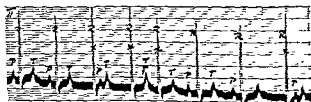


FIG 89 Nodal Escape The third, fourth and eighth complexes arise from the A-V node The fifth complex (*) is a response to P_1

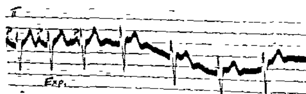


FIG 90 Nodal Escape As the vagus slows the heart on expiration, the auriculo ventricular node escapes The P waves are then buried.

suggesting a shift of the pace-maker Nodal rhythm may

are considered

CHAPTER 8

BRADYCARDIA AND DISORDERS OF *CONDUCTION*

BRADYCARDIA

Vagal effect. The rate of formation of impulses at the sinu-atrial node is slowed by an increase in vagal tone. This happens naturally in expiration particularly in young people; or it may occur in phases apart from breathing This variation is met with after fever, or from digitalis, and in jaundice

SINUS BRADYCARDIA. This is not uncommon in athletes and large men The rate is often 40-50 a minute, emotion, exercise and atropine will quicken it

SINU-ATRIAL BLOCK is present when a complete cycle is missed Without a tracing it may be difficult to distinguish this gap from true A-V block with dropped beats The electrocardiogram shows that the atrial (P) wave is absent (Fig 87) The intervals before the



FIG 87. Sinu auricular block

gap may be a little shorter than usual, and after it a little longer. Sometimes every other cycle is suppressed and so the rate is halved. Atropine will of course abolish this vagal abnormality, or exercise

Auricular standstill is very rare It may result from the toxic effect of digitalis, quinidine or potassium intoxication (Fig 124)

Nodal rhythm. The A-V node may replace the S-A node as pace-maker The rate is usually slow, about 50 a minute. In the cardiogram the P waves tend to follow the ventricular complexes As the direction of spread is reversed (from node to auricle), the P waves are usually negative (Fig 88). Sometimes they are hidden by the ventricular deflection Occasionally nodal rhythm may last for a long period in young people More often it appears as nodal

Wenckebach periods with dropped beats have been found in healthy subjects; these were abolished by atropine, or by increasing the sympathetic tone on exercise (4) Profuse salivation has been noted with these disturbances as a sign of high parasympathetic tone (5). It is possible that reflex increase of vagal tone explains the association between defects in conduction and disease of the gall-bladder (6, 7).

VASCULAR LESIONS In elderly people obliterative processes in the arterioles, accompanied by replacement fibrosis, may cut off the blood supply to the bundle, and thus depress its function, or cause it to degenerate In fact coronary disease is the most common cause (6) It is the posterior infarct of the left ventricle which usually damages the A-V bundle (8, 57) (p 264). Many cases are associated with hypertension Here again it is the common obliteration of the arterioles which starves the bundle, and gross coronary disease is common in these cases too

TOXIC AND INFLAMMATORY CAUSES The myocarditis of acute rheumatism is liable to cause A-V block Latent block is common in the acute phase, dropped beats and complete block may occur As atropine may temporarily abolish the block when given in a very large dose by intravenous injection, the vagus must be partly responsible In the past diphtheria was a serious cause of heart block Any local infection, e g in the nasal sinuses or in the lungs or elsewhere, may cause it It has been found in severe anæmia, and also in hyperthyroidism In both these conditions the delay has improved with therapy

CONGENITAL DEFECTS It has been supposed that there was an association between the ventricular septal defect of Roger's disease and complete heart block It has been found in complete transposition of the viscera (9) Incomplete heart block in some cases has been thought to be congenital in origin (10) An absence of the [illegible]

DRUGS Digitalis intoxication is not very common it should not occur of course Digitalis depresses conduction, directly and through the vagus As a cause of complete block it is very rare, but the delay clears up (6) (Fig 93 and Fig 129.)

Temporary heart block has been noted [illegible] angiocardia- [illegible]

[illegible] P-R interval

[illegible] possible to subdivide the time taken by the

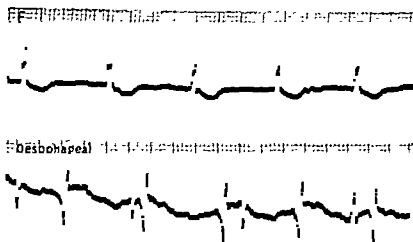


FIG. 91. Shows nodal rhythm with complete retrograde A-V heart block. Ventricular rate 80. Auricular rate 60. Œsophageal lead shows auricular intrinsicoid deflections.

AURICULO-VENTRICULAR HEART BLOCK

When there is delay or impairment in the conduction of the cardiac impulse from the auricles to the ventricles, heart block is said to be present In the *first degree* the impulse is delayed, so that the P-R interval is longer than 0·20 sec This is "latent block." The *second degree* of heart block, "incomplete" or "partial heart-block," is marked by the failure of some impulses to pass, causing "dropped beats" Two forms are distinguished: Type I, the milder, in which the P-R interval becomes longer before the failure to conduct (this is the "Wenckebach period"), and Type II where every second or third beat fails, without any lengthening of conduction beforehand This form has been associated with the name of Mobitz (1924) *Third degree block* is complete, so no impulses pass, the auricles and ventricles beat in dissociation

Causes. *Vagal effect.* Stimulation of the carotid sinus reflex may depress conduction through the action of the vagus Tumours in the neck or thorax may irritate the vagus and cause complete dissociation, or there may be absolute cardiac standstill, auricular and ventricular, a form of sinu-auricular block, sometimes for many seconds (*1*, *2*). A prolonged P-R interval over 0·24 sec was sometimes found in healthy candidates for flying On standing up the conduction was shortened to normal, and also by deep breathing (*3*). Even

TYPE I WENCKEBACH PERIODS The dropped beat may follow a cycle of progressive lengthening of the P-R interval until an atrial impulse is blocked In this way every third or fourth impulse may fail After the dropped beat the conduction improves, and may be



FIG 93 Dropped beats Alternate impulses are blocked, causing 2 1 heart block. P-R is prolonged to 0 32 sec. Ventricular rate between 50 and 60 Depression of T waves indicates the effect of digitalis, which has caused the block.

normal (Fig 94) The most severe variety is *2.1 block here the* [illegible] (Fig 93) The increasing



FIG 94 Dropped beats The auricular rhythm is regular (P) *but heart block causes prolongation of the P-R interval until* the third or fourth is blocked P tends to be merged in the preceding T wave, and alters its shape.

or perhaps progressing to complete block In *Type II* the impulse fails to pass without any previous prolongation of the P-R interval Every second, third or fourth impulse may fail to be accepted by the ventricle (Hay 1906, Mobitz 1924) In this group it seems that the lost impulse is due to a depression in the excitability of the [illegible] plete block with Stokes-Adams' *attacks (24)*

node and down the bundle to the ventricles Measurements in the electrocardiogram are taken from the beginning of auricular systole to the beginning of ventricular systole (Q or R or QS). Various leads should be measured as there may appear to be some variation The limb leads provide the clearest waves. The average P-R interval is about 0·16 sec. It varies with the size of the individual and the rate of the heart. In young infants it is usually below 0 12 sec.; in children it seldom exceeds 0·19 sec., but may do so if the vagal tone is strong. The effect of standing up on a prolonged P-R interval in an apparently healthy person has already been mentioned In large men with slow hearts the P-R interval may exceed 0 20 sec, but generally speaking anything longer than this is considered pathological, although a small increase by itself should not be taken to mean disease of the heart

Alternation of A-V conduction in the degree of block has been noted (58)

Diagnosis. This almost always depends on the electrocardiogram. Sometimes the sound of auricular systole can be detected, well apart from the following first sound, causing a third sound to be audible

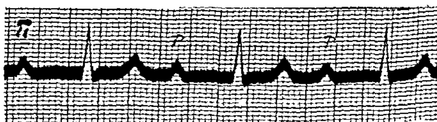


Fig. 92. Lead II, showing prolongation of P-R interval to 0 41 sec

When latent heart block occurs in mitral stenosis an appreciable interval may be detectable between the presystolic murmur and the mitral first sound. In latent heart block the P-R interval may reach 0 40 sec. or even 0 60 sec before beats are dropped Usually it is about 0 30 sec, it may remain constant at this level for years, sometimes it gradually increases (Fig 92)

Incomplete heart block with dropped beats (second degree). Two types of this block may be distinguished It should be remembered that the "dropped beat" can only certainly be recognised by auscultation of the heart, premature beats may not reach the pulse at the wrist, but they can usually be heard (Fig 93). Blocked atrial premature beats and sinu-atrial block are indistinguishable clinically from A-V block.

stroke volume elevates the systolic pressure; the systemic pulse pressure is usually large, and so is the pulmonary artery pulse pressure (55). In elderly patients, without sign of congestive failure, the pressures in the right side of the heart were raised; the systemic and pulmonary vascular resistances were increased, and so was the arteriovenous oxygen differences If there was obvious failure these abnormalities were worse (56). A bradycardia of, say 35, may be due to complete block or 2:1 block The important sign is the variation in the loudness of the first heart sound The sudden accentuated booming sound has been called the "bruit de canon." It occurs when the atrial systole is very close before the ventricular This phenomenon may be a summation effect, or due to the mitral and tricuspid leaflets being low in the ventricle, and then being stretched up hard to meet together (14) In the long diastoles the sounds of atrial systole are sometimes heard if the patient is thin, varying in position in the cycles (Stokes 1854) Incoordinate pulsations are seen in the veins in the neck, having no fixed association

made out in a constant position between the beats

Electrocardiograms are diagnostic (Fig 95) The auricular rhythm is often slightly irregular, for the P-P intervals with ventricular contractions between them are shorter than those without The shorter intervals are said to be due to the drag of the contracting ventricle, the longer due to a vagal effect *(16)*. On the screen the different auricular and ventricular rhythms can be made out as a rule The angiocardiogram shows that the atria do not empty every time they contract, there may be regurgitation into the pulmonary veins, and into the venæ cavæ *(17)*

The ventricular complexes often show the pattern of bundle branch block (Fig 99), the two types occur about equally (6). The reason for the prior activation of one side may

Males largely predominate, the ages of patients mostly range between 40 and 70 years

Transition *from partial* to complete block. Permanent complete block may be preceded by sudden erratic syncopal attacks due to ventricular standstill. During the phase of recovery the

The distinction of these two types is useful, for their prognosis is different. Exercise, by accelerating the auricle, will show that in Type I the degree of block is reduced if an electrocardiogram is taken at once. An intravenous injection of atropine (1/30 gr.) has the same effect. The effect of this is short so the curve must be taken quickly With Type II the block is increased when the auricle is accelerated, and 2:1 block may increase to complete block (*14*) While in Type I Stokes-Adams' attacks are fairly uncommon spontaneously, standstill of the ventricles can be induced reflexly by vagal stimulation, through the carotid sinus or by some visceral cause. Actually vagal slowing of the auricle in Type II may indeed reduce the amount of block from 2:1 to normal conduction, so in fact the pulse is accelerated by pressing on the carotid sinus (*14*)

Complete heart block. The atrial and ventricular rhythm are dissociated (Fig 95) The ventricles now beat to an idio-ventricular

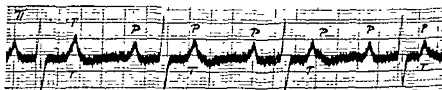


FIG. 95. Complete heart block. Note slow alteration in time relationship of P and ventricular complex. T waves are distorted by superimposed P waves

rhythm The site of the new pace-maker is usually in the junctional tissues just below the block *The rate is usually 30–40 beats a minute*, but examples of 25 or 50 are not uncommon. The rhythm is regular unless there are ventricular premature beats The rate is very *little affected by exercise, emotion, fever or amyl nitrite*. This is the fixed type keeping within a range of 8 beats per minute, awake or asleep But there are two others with labile variations, one *quickening and slowing and the other with sudden variations* in the site and rate of impulse formation. Atropine abolishes these changes, and exercise may cause them They are precursors of fibrillation (*15*) *If the centre is in the upper levels of the bundle it* is probably to some degree under vagal influence, since a large (1/30 gr) intravenous injection of atropine may cause some acceleration If the *initial rate is high, the increase in rate is more* Adrenalin has little effect on the rate unless it is low (*14*). In complete block the heart meets the extra needs of the body by increasing the stroke volume *But in spite of* this the output tends to be low. This increase in

(20, 21) (Fig 97) Ventricular tachycardia may change to fibrillation, and vice versa (16) The attacks *occur in* rather over half the cases of complete block (6) In a fifth the attack may be the first evidence of illness Their frequency varies, it is highest when there is coronary disease (6) The duration and severity also varies much, from slight weakness and dizziness to complete syncope.

CLINICAL FEATURES. In the mildest attack, as stated above, a transient weakness, giddiness, or confusion is all. In the full-dress



FIG 97 Stokes Adams' attack Lead II shows ventricular fibrillation Note varying size and shape of ventricular com plexes Leads I and III show complete heart block Q T time is prolonged

attack there is sudden loss of consciousness, the *patient* has practically no warning He may fall and hurt *himself*. Pallor at first, is later followed by cyanosis, or a flush, as the circulation returns The breathing becomes *stertorous* The muscles are at first relaxed then there may be *twitching* and convulsive movements particularly of the arms, the eyes stare and are rolled up The pulse goes and the heart *stands still* (unless there is ventricular tachycardia and in those cases when the ventricular rate has fallen to 10 or 12 a *minute*) Once the circulation is restored, then recovery is rapid, and the patient is himself again in a few moments, continuing, perhaps, an *interrupted* conversation (Fig. 96) During the syncope there may be a passage of urine and fæces Attacks may come for years, or there may be long periods of freedom· but one day an attack is usually fatal

bradycardia of complete block may be noted as a characteristic sign (14) In Type II block there may be syncope following tachycardia of atria when there was 2:1 block, or with a very severe degree of bradycardia or with ventricular fibrillation (14).

Myocardial infarction sometimes causes complete block when the infarct is posterior or septal (57). The rate is often relatively fast, about 60 a minute. If the patient survives, recovery of conduction is not uncommon; but there is a high immediate mortality (6) But it is not higher once the early phase is past; about half are alive at the end of a year (57)

SUPERNORMAL RECOVERY PHASE. This term was used by Lewis to explain the fact that immediately after recovery from the refractory period, heart muscle may respond to stimuli which are below the normal threshold strength In some instances complete block occurred when the auricular rate slowed, and conduction was not established until a ventricular beat came just before an auricular wave. Conduction was kept up till the interval between the auricular beats exceeded 1·0 sec Conduction then failed until a suitable time relationship came again Adrenalin may provoke such convenient ventricular beats (Fig. 96)

The Stokes-Adams' syndrome. The auricles continue to beat, although after 20 sec of ventricular standstill they are affected by anoxia Then the beating is slower and irregular, flutter or fibrillation may come on, or all movement cease (Fig 96) The attacks are

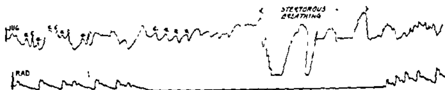


FIG. 96 Tracing of jugular and radial impulses during a Stokes-Adams' attack, lasting 16 sec Auricular contractions (a) can be seen in the jugular tracing until obscured by stertorous breathing, which ensues in 8 sec.

common when partial block is becoming complete, before the idioventricular rhythm is established The changing of the type of ventricular complexes in the course of partial or complete block may indicate that the onset of standstill is likely Here attacks are likely to be recurrent and fatal When there is complete block syncope may be due to ventricular tachycardia, flutter or fibrillation, a very

block is also a contra-indication (32), certainly for intravenous injection (33) Procaine amide (pronestyl) and quinidine are too prone to depress the conducting tissues, and so are not to be used in heart block Isuprel may be useful in stimulating higher ventricular centres in the ventricles when there is tachycardia (22). In fact procaine amide may cause fibrillation if there are premature beats or an intraventricular defect in conduction (34). It is clear that no effective and safe remedy is available when these disturbances occur with complete heart block

(iii) There is of course no risk in giving digitalis if there is failure with complete block Isopropyl norepinephrin taken by mouth may raise the rate a little and so improve the circulation (56)

(iv) *Latent first degree block* does not, in itself, require treatment If there is failure digitalis may increase block, or actually reduce it

(v) [illegible]

[illegible] spreads back to the atrium as well as forwards to the ventricle *This causes inverted P waves immediately after or before the QRS Complex* Sometimes there may be progressive delay in the time of the [illegible]

period

form o

Here [illegible] gradually diminish and end in a normal conduction of impulse (35)

RECIPROCAL RHYTHM (Drury 1924) describes a condition in which the retrograde block delays the impulse spreading to the atrium, so that it can pass back to the ventricle which will no longer be refractory The sequence of events is that one impulse from the node may give rise to two ventricular beats This may happen every other beat or every fourth or fifth beat (Fig 99) [illegible]

[illegible] There is therefore dissociation, but the ventricular rate is faster than the auricular There is *complete* retrograde block unless an auricular beat occurs just at the end of ventricular systole and the supernormal recovery phase allows the ventricle to respond (Fig 100 (a)) This is a transient derangement Recovery will pass through reciprocal rhythm and latent block (Fig 100 (b))

Treatment. This aims at stopping an attack and preventing more. *The means to be used depend on whether there is standstill,* or threatened standstill, of the ventricles, or ventricular tachycardia or fibrillation. Unfortunately the information is not always available In one stimulants are needed, in the other depressants

(i) For *ventricular standstill*, the sympathetico-mimetic drugs are wanted. If the heart has stopped adrenalin must be injected into it; 5 minims of the 1:1000 solution. If the rate has only fallen very slowly, 10 minims of the drug may be given hypodermically, and may be repeated as needed. Ephedrine ($\frac{1}{2}$ gr.) by mouth is slower and more prolonged. Isuprel (isopropyl norepinephrine) can be taken under the tongue (20 mg every 4–6 hours is useful) *(22)* There is

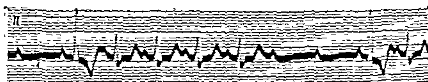


FIG 98. Stokes-Adams' disease. Effect of adrenalin. Note short runs of normal beats which begin with a premature ventricular systole, and continue until the auricular rate slows.

no pressor action *(24)*. Isuprel may be given intravenously, 1 mg. in 200 ml of 5% glucose in water at the rate of 10–20 drops a minute *(25)* Noradrenalin has been suggested by intravenous injection (0 02 mg) or by hypodermic injection 0 2 mg. every 40 minutes *(26)*. Adrenalin is probably better for persistent and recurrent seizures due to standstill. Given by intravenous injection, 5–44 mg per minute, it is useful, but may raise the blood pressure *(27)* The rate may rise above 50 and extrasystoles appear (Fig 98) There has been some success with an electrical pace-maker This is likely to be useful if standstill occurs at operation where it can be ready for immediate use *(28)*. The stimulus was up to 60 volts 20–200 times a minute *(25, 26, 29)*.

Sodium lactate in molar solution, 250 ml given in 30 minutes by intravenous injection at about 15 ml a minute, has helped to correct very slow rates and prevent standstill *(30)* The solution may be used in half molar strength *(31)*

(ii) For *ventricular tachycardia or fibrillation* the depressants should prove useful; these are quinidine and procaine amide. But, in fact, they can be dangerous. If there is tachycardia both of these may cause fibrillation if there is complete heart block. Bundle branch

curves. By vectorcardiography the loop in the horizontal plane
may lie a
slowing,
cases wi
vectorcardiogram passing to the left and slowing at its end towards

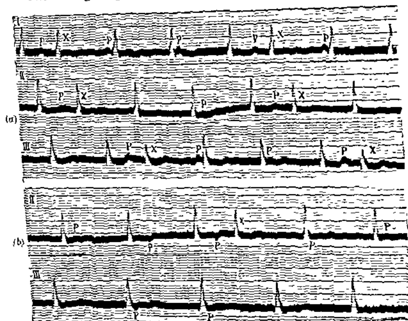


FIG 100 (a) Interference dissociation Note upright P waves at a rate of 64, with a ventricular rate of 100 Early beats (marked X) are clearly seen when P and T summate (b) Reciprocal rhythm Lead II First complex shows dissociation with upright P in S-T interval The second shows partial retrograde heart block with inverted P (R P = 0 24 sec) Third complex similar. This is answered by the fourth R (marked X) which is reciprocal rhythm Fifth and sixth complexes show complete dissociation Lead III Nodal rhythm.

the right, showing delay in depolarisation Thus the VCG helps to distinguish two types (39) Infarction of the septum more often causes the right-sided lesion than the left (39) There is a high incidence of coronary disease in both types, and the masking of the infarction curve by the left-sided bundle block is a well-known source of difficulty (p 253) Some cases are due to rheumatism (40),

The opposite condition is seen when orthograde conduction is blocked, and retrograde conduction persists in complete A-V block Here inverted P waves appear in the S-T interval These disturbances may be closely allied Quinidine delays retrograde spread Amyl nitrite may cause nodal rhythm (36)

Bundle branch block. There is delayed activation of the affected ventricle, left or right. In the case of the left-sided defect the lesion

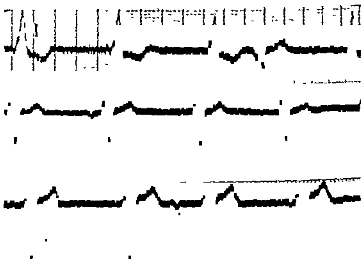


FIG. 99. Reciprocal rhythm with a reversed Wenckebach period of five cycles of retrograde heart block A cycle begins in the second complex of lead II with an inverted P preceding the QRS by 0 12 sec. In the fourth complex an inverted P occurs in the S-T period with an R-P interval of 0 28 sec. In the second complex of lead III the R-P interval is 0 48 sec This P is answered by the succeeding beat, the P-R interval being 0 28 sec. Left bundle branch block is also present

is usually found on histological examination But this is not the case in the patients with partial right bundle block, where there is a minor degree of delay only. If the delay is complete then a local lesion may be detected (37) But some right-sided lesions are probably congenital, and certainly benign and quite unassociated with any myocardial disease. There is a good deal of reason to suppose that hypertrophy of the right ventricle may be responsible for some curves of this type (p 55) That delayed depolarisation of the right side may not be present is shown by cardiac catheter pressure

heart, vertical or horizontal *Left bundle branch block.* If the block is on the left side the negative intrinsicoid deflection (Q or QS) occurs at once in the leads over the right ventricle the moment the

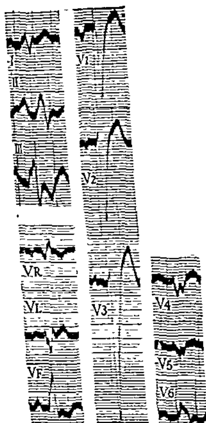


FIG 103 Left bundle branch block with vertical heart.

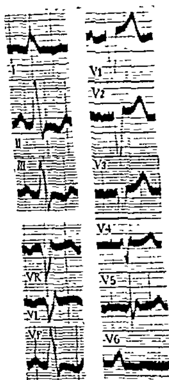


FIG 104 Left bundle branch block with vertical heart Standard leads are of th concordant type

impulse reaches its surface (V1 and V2) A tiny R wave may pr cede it Over the left ventricle, in V5 and V6 the intrinsicoid defle tion is late, perhaps at 0 08–0 10 sec (Fig 101) In the *right bun branch block* type of curves the intrinsicoid deflection is delayed V1 and V2 leads, giving an rsR pattern (Fig 102) In V5 and V6 it

where fibrosis involves the main branch, or is scattered through the ramification. The right-sided pattern is common with atrial septal defect (p 54).

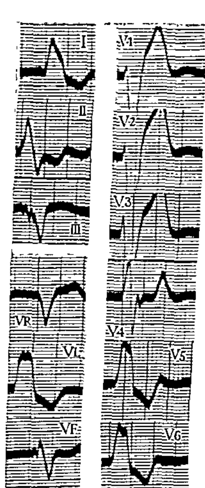


FIG 101 Left bundle branch block. The heart is horizontal Note early intrinsic deflection in leads V1 and V2, and delayed intrinsic deflection in V5 and V6.

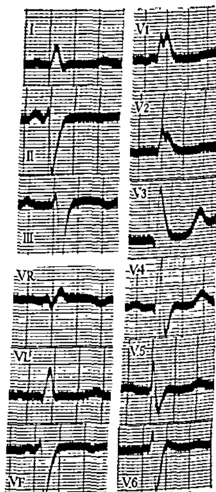


FIG 102 Right bundle branch block Note intrinsic deflection delayed on right side of septum by 0 16 sec It is early on the left. There is complete block.

The electrocardiogram. This is essential in the diagnosis QRS is prolonged, usually up to 0 12 to 0 16 sec The precordial leads are most reliable in showing on which side is the delay in depolarisation The limb leads vary a great deal with the position of the

(Fig 106). When ventricular extrasystoles occur in bundle branch block, the QRS be of normal duration if they come in the supernormal phase of ventricular recovery (*41*) (Fig. 107)



FIG. 107 Incomplete right branch block (QRS 0 10 sec) showing restoration of normal rhythm

Lead I Nodal rhythm at rate of 100. No *evidence of* auricular activity

Lead II Nodal rhythm. P waves deform S-T interval of alternate complexes

Lead III P waves move forward from S-T till S.A node takes control at fifth complex *when QRS* returns to normal

Left bundle branch block (QRS 0 14 sec) now established, but transitional complex follows the compensatory pause after a premature contraction in lead I

PARTIAL BUNDLE BRANCH BLOCK is analogous to partial A-V block with dropped beats It is a rare finding The curves may appear intermittently, or be transient.

How far these curves showing delayed activation of the surface

immediate (Fig. 102). The effect on the left-sided type of the vertical position on the limb leads, where the left leg records the potentials from the left ventricle, is shown in Figs. 103 and 104. Usually the

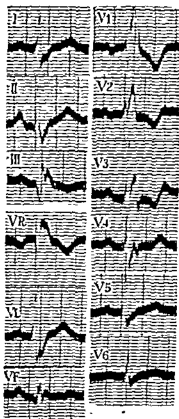


FIG 105. Right bundle branch block. Wide S_1 pattern The intrinsic deflection is late in V1 to V3 and early in V4 to V6

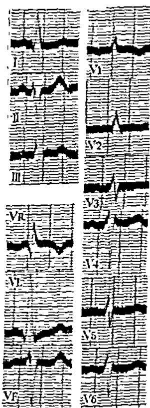


FIG 106 Incomplete right branch block Note small R waves with delayed intrinsic deflection on right side QRS 0 10 sec There is left axis deviation and the heart is horizontal

[illegible] ement The effect [illegible] ht-sided pattern [illegible] from the right is shown in Fig 105. Usually the [illegible] ventricular enlargement often present in those cases

INCOMPLETE BUNDLE BRANCH BLOCK This term has been used for curves when there are minor degrees of delay in one bundle

has been sought. in some cases it was found but not in others As a rule the right receives the impulse before the left, so that there is pre-excitation of this chamber, and delayed activation (relatively) of the other The curves therefore are of the left bundle branch type as a rule (Fig 108). But the P-S interval (i e. P-R + QRS) is normal in W.P.W. and over 0 26 sec in bundle branch block (46) If there is actually real left bundle block the pre-excitation of the unaffected ventricle can be recognised (47) A case recorded with multiple complicated arrhythmias supported the by-pass theory (48) There has been some support on anatomical grounds of such a pathway (49). Holding the breath may change the curve to normal, or the reverse (59)

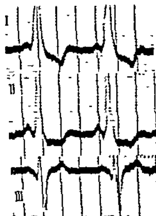


FIG 108. Wolff Parkinson White syndrome Lead I, P R interval is 0 08 sec QRS is 0·14 sec.

The alternative theory is that an irritable focus is the cause Rather similar premature beats have been found during cardiac catheterisation, possibly arising just below the A-V node (50). The curves have been seen after the intravenous injection of strophanthin (51) Perhaps they are the result of ventricular extrasystoles coming just immediately after atrial systole Cardiograms from inside the ventricular cavities show both types, left and right The conclusion was that there was a hyper-excitable centre near the node. when there was sinus rhythm this was stimulated by atrial systole, but not mechanically, for it is active when there is fibrillation (52) Premature contractions of the W.P.W type may appear in arteriosclerotic heart disease They may be associated with serious ventricular arrhythmias (53) [illegible]

[illegible] one there may be an extra pathway or increased rate of A-V conduction, and in the other an irritable focus, perhaps associated with disease The presence of this curve may mask the patterns of an infarct, which may become apparent if the W P.W curve disappears There is a high preponderance of males, 70% The abnormality is not associated with any congenital

of one ventricle are due to a local bundle lesion or to a general enlargement of the whole ventricle, or depression of its function as a whole, cannot be told from the electrocardiogram. Additional evidence is needed, particularly from the vectorcardiogram.

TRANSIENT BUNDLE BRANCH BLOCK. Sometimes the abnormality is transient, although it usually persists. After diphtheria recovery is usual. recovery is less frequent in rheumatism and infarction. After pulmonary embolism the right-sided lesion may be transient. Temporary branch block may last for days or weeks in congestive failure. Slowing of the rate by carotid sinus pressure may restore normal conduction.

BILATERAL BUNDLE BRANCH BLOCK. This may mean that the curves of block appear on right and left sides alternately. A-V conduction is prolonged, the intrinsicoid deflection is later on the more affected side (*42*).

Masquerading bundle branch block is the name given to the appearance of a left-sided lesion in the limb leads, and a right-sided in the precordial. It is thought in fact to be left-sided (*43*). The PR interval may be lengthened, it is certainly pathological and may show bilateral damage, probably ischæmic in origin (*44*)

Clinical diagnosis. This cannot be made with any certainty The asynchronous contraction of the ventricles may cause a double apex thrust and a double first sound; or widely split first sound. But this kind of ventricular contraction may be present without the characteristic curve and the curve may be present without the signs In the same way the second sound may also be double at the base. but again correlation is inconstant There are no symptoms It is possible that when patients with bilateral bundle branch block get syncopal attacks, these are really Stokes-Adams' seizures (*45*) (p 392)

Course and prognosis. There is no interference with the efficient working of the heart The effect and prognosis depend on the associated lesion or lesions In the large majority of cases the heart is enlarged; many have developed failure The right-sided lesions often seem less grave than the left But the associations are so variable it is best to give it no prognosis at all, and consider rather the other features of the case.

Short P-R interval and bundle branch block type of QRS. (Wolff-Parkinson-White Syndrome) Complexes suggesting bundle branch block may be found which are associated with a P-R interval of less than 0·12 sec. It seems possible that an accessory bundle activates one ventricle before the other and anatomical confirmation

has been sought: in some cases it was found but not in others. As a rule the right receives the impulse before the left, so that there is pre-excitation of this chamber, and delayed activation (relatively) of the other. The curves therefore are of the left bundle branch type as a rule (Fig 108). But the P-S interval (i.e. P-R + QRS) is normal in W.P.W. and over 0.26 sec. in bundle branch block (*46*). If there is actually real left bundle block the pre-excitation of the unaffected ventricle can be recognised (*47*). A case recorded with multiple complicated arrhythmias supported the by-pass theory (*48*). There has been some support on anatomical grounds of such a pathway (*49*). Holding the breath may change the curve to normal, or the reverse (*59*).

The alternative theory is that an irritable focus is the cause. Rather similar premature beats have been found during cardiac catheterisation, possibly arising just below the A-V node (*50*). The curves have been seen after the intravenous injection of strophanthin (*51*). Perhaps they are the result of ventricular extrasystoles coming just immediately after atrial systole. Cardiograms from inside the ventricular cavities show both types, left and right. The conclusion was that there was a hyper-excitable centre near the node; when there was sinus rhythm this was stimulated by atrial systole, but not mechanically, for it is active when there is fibrillation (*52*). Premature contractions of the W.P.W. type may appear ...



FIG. 108. Wolff-Parkinson-White syndrome. Lead I, P-R interval is 0.08 sec. QRS is 0.14 sec.

... in the one there may be an extra pathway or increased rate of A-V conduction, and in the other an irritable focus, perhaps associated with disease. The presence of this curve may mask the patterns of an infarct, which may become apparent if the W.P.W. curve disappears. There is a high preponderance of males, 70%. The abnormality is not associated with any congenital

lesion. The only clinical sign is that the mitral first sound is sometimes split (*46*). It is common to find tachycardia, auricular or ventricular in the patients with this sort of curve. If there is myocardial infarction tachycardia is very likely and may be grave. In any case about 70% of cases with the syndrome have paroxysms of tachycardia (*46*) (p. 332). The important thing is to distinguish this curve from that of bundle branch block. In itself it is not important. In both it is the associations that matter.

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CHAPTER 9

TACHYCARDIA

During the last decade doubt has been cast on the validity of the theory of circus movement. The matter is not yet settled, but, if auricular fibrillation and flutter are due to the activity of a single ectopic focus, the subjects considered in this chapter will be brought into closer relationship than was formerly thought to be the case Auricular premature systoles, auricular tachycardia, auricular flutter and fibrillation would differ only in the speed of the impulse formed in the centre Ventricular premature systoles and ventricular tachycardia are due in the main to ectopic ventricular foci, although *re-entry of the stimulus plays a part in some cases. The rapid* strides in cardiac surgery have made us more familiar with ventricular fibrillation The causes of this lethal complication are still uncertain but methods of combating it have been devised. In many complicated arrhythmias the œsophageal lead furnishes information not provided by any other lead, and fuller exploitation of this lead in the future may obviate the need for much painstaking and dubious analysis of these arrhythmias from the conventional leads.

Sinu-Auricular Tachycardia

This is sometimes called physiological tachycardia since it is not due to any abnormal rhythm in the heart It occurs in a variety of conditions, of which only a minority are associated with disease of the heart

Myocardial Failure Tachycardia occurs in heart failure The stroke volume diminishes, so the rate may increase in order to maintain the minute volume But the mechanism is by no means clear. As the contraction of the heart becomes more efficient with treatment, the rate slows.

Peripheral Circulatory Failure. In shock the volume of venous blood returning to the heart is diminished and the rate of the heart increases in order to attempt to maintain the output The reason for this is obscure

Infections. It is well known that in fever the pulse rate rises about ten beats for each degree of rise in temperature. Sometimes the tachycardia is out of proportion to the temperature. Many of

these have acute myocardial lesions, such as infarcts, rheumatic heart disease or pericarditis. Peripheral circulatory failure, associated with a low blood pressure, is also the cause of the disproportionate tachycardia which occurs in some cases of pneumonia. Myocarditis was found in some fatal cases of poliomyelitis where tachycardia had been prominent (*1*)

Tachycardia may occur if sufficient rest has not been allowed after an acute infection, this may lead to the development of a cardiac neurosis, which may cause the tachycardia to persist.

HYPERTHYROIDISM causes a persistent tachycardia. The subject is discussed in Chapter 6

ANXIETY NEUROSIS Tachycardia is frequently found in anxiety. The patient complains of palpitation Other symptoms are: breathlessness, fatigue, left submammary pain and dizziness Sweating in the axillæ, and of the palms of the hands and soles of the feet is common, but is found in other patients Moderate exercise increases the rate a little, and in some cases it may even fall during the first few minutes after the exercise The syndrome, originally described by

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doubt has been induced as to the integrity of the heart, sometimes through the accidental finding of a murmur, and this has generated a fear of sudden death on exertion Often

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HYPERINSULINÆMIA. In some cases symptoms occur only two or three hours after meals They comprise tachycardia, choking pain in the chest, tremor, muscular weakness and occasionally fainting The attacks can be reproduced by injections of 10–15 units of insulin

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tolerance curve falls sharply. The symptoms are probably due to the release of adrenaline to combat the falling blood sugar. They are best treated

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The Œsophageal Lead

TECHNIQUE. An œsophageal electrode can be constructed from a Ryle's duodenal tube. The bulb at the end is replaced by an electrode of German silver; wires running up the bore of the tube connect this to a terminal which is attached to the chest electrode from the patient's cable. The tube is either swallowed or introduced along the nares; most patients find it easier to swallow. It is passed down into the stomach and then withdrawn a centimetre at a time until sharp auricular intrinsicoid deflections are seen This normally happens at a level of between 30 and 50 cm. from the lips. Difficulty is sometimes experienced in obtaining a steady base line. Twisting the tube may obviate this as better contact may thus be secured (2) Another method is to use a tube with a small exit instead of the German silver electrode and flush through continuously with normal saline (3).

NORMAL RECORDS The œsophagus is in close relationship with the left auricle for about 5 cm. below the level of the sixth dorsal vertebra, lower down it lies behind the diaphragmatic surface of the ventricles The impulse spreads radially from the sinu-auricular node at the anterior margin of the junction of the superior vena cava with the right auricle, but also from above downwards. The inferior region of the left auricle and the left auricular appendage are the last to be activated (4) At the ventricular levels, as the tube is withdrawn from the stomach, an upright P is seen. The ventricular deflections resemble those of lead F As the tip approaches the auricular zone, P becomes more peaked and narrow, until the sharp auricular R appears At the upper auricular levels where the tip is nearer the sinu-auricular node, the descending limb of R is prolonged into an S wave and finally R disappears. At this level the ventricular deflections show a large Q with a small R and negative T which represent the potentials of the cavity of the left ventricle At supra-auricular levels the auricular S wave becomes blunted and finally resembles the negative P of lead R. The size of the auricular intrinsicoid deflection may reach a total of 25 mm. (5), although the average is about 6 mm. The stretch at which they appear varies greatly in different patients. The longest was 22 cm while in some they were seen at one level only (2) The auricular QRS has a duration of about 0 06 sec.

The auricular T wave is seen best in patients with complete heart block since, when the rhythm is normal, it coincides with the ventricular deflection. The auricular T is a broad shallow deflection which is

opposite in sign to the major initial deflection The Q-T interval is about 0 36 sec.

Premature Systoles

Premature systoles may arise from the auricles, the A-V node or from the ventricles Exceptionally they may come from the S-A node. The irritable point in the heart muscle initiates a contraction before the normal impulse from the sinu-auricular node has reached it.

A premature beat is weak, as the ventricle is incompletely filled at the moment of contraction The strength of the contraction depends upon the prematurity of the beat. Pressures of ventricular premature beats recorded while a catheter was in the right ventricle showed that those which occurred during the ejection phase of the preceding beat cause only a broadening of the systole of that beat, and maintained the diastolic pressure [illegible]

diastole showed a normal systolic pressure. In all but the late premature beats there was an increase in the latent period between the electrical and the mechanical response. This is probably due to refractoriness of the myocardium (6) The premature beat may, or may not [illegible]

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The [illegible] normal beat—the returning beat—is usually stronger than normal The premature contraction can be heard at the heart, except in rare instances of blocked auricular premature systoles, and the diagnosis is best made by auscultation, in order to differentiate this irregularity from true dropped beats of heart block. Beats that fail to cause a pulse wave may only give the first heart sound for the valves will not open; otherwise both sounds are present The first sound of a premature beat [illegible] er of [illegible]

[illegible] under

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[illegible] of the P wave. This is because the auriculo-ventricular valves descend during the period of rapid flow of blood into the ventricle and [illegible]

have further to tra[illegible]

ventricular systole [illegible] they are moving fast

and so vibrate more strongly (7).

Premature systoles are not common when the rate of the heart is

over 110 a minute, so acceleration of the heart by exercise may abolish them. When they are present at this rate the muscle is usually diseased.

Auricular premature systoles. The P wave in the electrocardiogram is premature; it may be inverted, biphasic, or of a size different from that of the other P waves in that lead, or be superimposed upon the preceding T wave. The variations from the normal are best seen in the œsophageal lead, where it may be obvious that the early beat is ectopic through having a predominant S wave at the lower auricular levels, otherwise chest leads reflecting the potentials of the right side such as V1 or V2, or leads II or F may be used. In most cases the succeeding ventricular complex is altered either in regard to the height, direction or duration of the QRS, or of the height or direction of the T wave. Aberration indicates incomplete recovery of the conducting tissues. Aberrant conduction *is more likely to occur if the preceding cycle is long as the refractory* period is then prolonged In bigeminy due to auricular premature systoles the first only may show an aberrant response *(8)* Exercise may abolish aberration by increasing the rate *(9)*. Occasionally auricular premature systoles may come within the supranormal phase and show normal conduction although the basic rhythm is that of bundle branch block *(10)* Prematurity is not the only factor, as aberration may appear during quinidine therapy, or during an attack of pneumonia when some toxic action on conduction must be presumed The P-R interval is often lengthened after an auricular premature systole Occasionally the impulse is blocked, and there is then no ventricular contraction.

The impulse from the premature auricular systole passes back to the sinu-auricular node and discharges the one which is forming there The rhythm of the heart is thus fundamentally disturbed *since a new impulse forms at the sinu-auricular node* The pause after an auricular premature systole consists of the normal interval between the beats plus the time taken by the ectopic impulse to spread to the S-A node *It is not so long as the full compensatory pause following ventricular premature beats Sometimes it is possible* to recognise this clinically

Nodal premature systoles. Nodal premature systoles are uncommon The impulse is generated at the auriculo-ventricular node, and spreads *downwards to the ventricles and backwards to* the auricles As in nodal rhythm the P wave is inverted, and may appear before the QRS, or be buried in it, or follow it The ventricular complexes are normal.

Ventricular premature systoles cause highly abnormal ventricular deflections of the same kind as in bundle branch block They are usually large and biphasic. If the main initial deflection is upward, the end deflection is downward; QRS is prolonged.

Premature ventricular systoles used to be divided into those arising from the right and left ventricles on the lines of bundle branch block Thus an upward initial deflection in lead I with a downward initial deflection in lead III would signify a premature systole arising from the right ventricle just as, if not premature, it would signify left branch block in which the right ventricle is activated first It seems more likely, however, that their shape is determined more by their relation to the apex and the base of the heart.

In any case the differentiation of premature ventricular systoles is of little clinical importance Thirty years ago the reversal of the formerly accepted interpretation made no difference to diagnosis or prognosis

Retrograde conduction to the auricle often occurs in ventricular premature systoles This was seen in 15 out of 33 cases in the

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pensatory pause' usually occurs, since the next impulse from the sinu auricular node finds the ventricular muscle refractory. The sum of the cycle before the early beat and that after it equals two normal cycles A compensatory pause may also be seen in cases with retrograde conduction as the sinus node may discharge before the retrograde impulse reaches it Ventricular premature beats with retrograde conduction to the auricle may be followed by escapes of the node (12) If the heart is beating slowly, and the ectopic impulse is very early, the ventricle may again be ready to contract by the time the normal impulse arrives. A true extra-systole then results which is spoken of as an "interpolated extra-systole" since the premature systole is interpolated between two normal beats The P-R interval following an interpolated extra-systole is usually prolonged, owing to fatigue in the conducting tissues If the P-R is much prolonged the "compensatory pause" may be postponed as the next beat may be dropped ... sinus impulse

wave may be
beat, after a

time (*14*). Premature systoles may provoke alternation of the pulse

MULTIPLE PREMATURE SYSTOLES may occur when several ectopic foci are active at the same time. If the rate is rapid, as it often is in these cases, the clinical irregularity may be difficult to distinguish from that of auricular fibrillation.

Ætiology of premature systoles. Premature systoles do not by themselves signify heart disease as they are frequently found in hearts which are otherwise normal. They occur more often in men than in women, and are increasingly common as age advances.

A normal heart may be irritated in a variety of ways. Digestive disturbances, particularly associated with heavy meals, and the excessive use of tea, coffee, tobacco or alcohol may lead to ventricular premature systoles. Injections of adrenaline can produce them, and psychological disturbances may act in the same way through stimulation of the sympathetic nervous system. Premature systoles may arise during the course of any acute infection

In myocardial disease premature systoles are often met with in active rheumatism They appear with ischæmic lesions, and also in acute focal inflammation. In rare cases they are seen in combination with malignant deposits, or in syphilis

Digitalis produces ventricular premature systoles when it is gi [illegible] which a [illegible] usually a [illegible] persist sometimes in patients on maintenance doses; then it may be disregarded There is evidence that premature systoles due to digitalis intoxication may be caused by disturbance in the potassium balance in the heart muscle, since they can be abolished by the administra- [illegible] stoles are more often [illegible] fibrillation

Nature of premature systoles. Single premature systoles can be evoked experimentally by induction shocks, or by means of mechanical or thermal stimuli Alterations in the quality or quantity of the blood supply may produce them. also stimulation of the autonomic nerves controlling the heart In certain conditions the heart seems peculiarly liable to generate premature systoles. Thus chloroform may induce a state in which premature systoles may be readily produced by many different stimuli

Parasystole. Premature systoles may recur at intervals over long periods. The intervals may be regular or irregular, but if irregular, a common denominator in units of time can be found to cover them all, if a sufficiently long tracing is taken. In these cases two centres in the heart muscle are actively producing impulses. The centre with the faster rhythm, which is usually the higher centre, is dominant, but the lower centre is protected from the impulses arising in the higher by a unidirectional block (Entrance Block). Thus there may be a centre in the ventricle which is generating impulses at a slower rate than the dominant sinus rhythm. It is protected from the normal sinus impulses by the block, but its own impulses can pass out to activate the rest of the ventricle. The heart, however, will not respond to impulses during the refractory period. Only those impulses from the ventricular centre which arrive while the ventricle is receptive will be answered. The result of this interplay of the two rhythms is that ventricular premature systoles occur at intervals which are usually irregular, since the rate of the lower centre will usually bear no simple mathematical relationship to that of the higher centre. If the rate of impulse formation in the two centres does not alter, however, the intervals between the premature systoles will be related to each other, since the three factors concerned in their appearance—the rate of the higher centre, the rate of the lower centre and the refractory period of the heart muscle are constant.

Rarely the rate of impulse formation in the ectopic focus is faster than that of the sinus rhythm. In these cases some of the ectopic impulse must also be blocked (Exit Block).

Complicated arrhythmias ensue when the parasystolic focus discharges only ...

... in a child of five years. Fusion beats, due to the almost simultaneous discharge of the two centres, were present (17).

Re-entry. Especially in digitalis intoxication a bigeminal rhythm may occur in which the ventricular premature systole is accurately linked in time to the preceding beat. Here it is probable that the premature systole is caused by the same stimulus as the normal beat. Th...

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fixed coupling of this type is more likely to be found after the longer cycles since the conducting tissue is then more refractory (*18*). In cases of ventricular parasystole in fibrillation, ventricular premature systoles with fixed coupling may follow only the ectopic beats, giving rise to an appearance of paired premature systoles opposite to each other in sign A unidirectional block causing the parasystolic centre to be refractory to impulses reaching it from the node yet receptive to impulses reaching it from the ventricle seems a likely explanation (*19*)

SYMPTOMS. Premature systoles are a cause of discomfort to many people They feel their hearts to be turning over, or else it seems to stop. The strong returning beat after a pause may be felt as an unpleasant thump. On the other hand, less sensitive individuals are often unaware of any irregularity

PROGNOSIS. Multiple premature systoles from several foci, especially when they are associated with a rapid rhythm, are not found in healthy hearts Otherwise premature systoles have no prognostic value of their own If there are cardiac lesions, they may have some bearing on the outlook of the case In mitral stenosis auricular premature systoles may point to the early onset of fibrillation. After a coronary occlusion ventricular premature systoles somewhat increase the gravity of the prognosis, by suggesting the possible development of ventricular tachycardia (see p 264)

Single premature systoles do not damage or overload the heart They may suggest the presence of lesions, but alone they have no more significance than a systolic murmur, or a pulse rate of 120

Treatment. Premature systoles usually require no treatment beyond reassuring the patient by telling him that they are of no importance in themselves Sometimes they may point to a source of toxin which is irritating the heart, and suggest a search for sepsis in the teeth, tonsils, sinuses, gall-bladder, urinary or alimentary tracts. If the premature systoles disturb the patient, the removal of coffee, tea, tobacco or alcohol may be effective in controlling them Bromide or phenobarbitone may abolish those associated with psychological disturbances Quinidine sulphate in doses of 10–15 grains daily will often reduce the number of premature systoles materially Both auricular and ventricular premature systoles can sometimes be checked by the use of small doses of digitalis Ventricular premature systoles produced by toxic doses of digitalis can be abolished for a time by potassium acetate in doses of 5 or 10 g. In cases of multiple premature systoles in myocardial disease, or premature systoles occurring in other forms of heart disease,

the treatment is that of the associated lesion Procaine amide (pronestyl) is worth a trial

THE AURICULAR TACHYCARDIAS

There ...

lar paroxysmal tachycardia is due to an ectopic focus situated in the auricles which produces regular impulses at rates which vary from 120 to 250 per minute. In auricular flutter, the flutter peaks have a rate of 250 to 360 and are regular ...

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to 500

and is an intermediate stage between flutter and fibrillation The flutter peaks are slightly irregular at a rate of about 350.

Ætiology of fibrillation and flutter. Nearly forty years ago Lewis propounded his well-known theory of Circus Movement to explain flutter and fibrillation. He considered that both were due to a circular wave involving in the case of flutter the orifice of the superior and inferior venæ cavæ From this central circulatory wave impulses spread out to all parts of the auricle This theory has recently been challenged The evidence at present is conflicting, both from the experimental and clinical aspect

There are four possibilities a single circus, multiple circuses due to re-entry of the stimuli, multiple ectopic foci; and a single heterotopic tachysystole

EXPERIMENTAL EVIDENCE Lewis traced the waves in flutter almost, but not completely, through a circle in dogs In human subjects he relied upon varying time relationships in electrocardiograms He assumed that the same process obtained in fibrillation because of the g... flutter in man

... flutter returns to both auricles (21) This work favours a single ectopic focus in flutter High speed cinematography in cases of flutter in man occurring during valvotomy has shown that both auricular appendages contract together which would be unlikely with a central circulatory wave (22) On the other hand in some cases during catheterisation

systolic waves at 230 were visible on the pulmonary artery tracings *and they preceded those of the right auricle. It is suggested that* they were due to the *impact* of the left auricle and that the contraction of the left auricle must therefore precede that of the right *(23)*.

A single shock applied at the vulnerable period at the beginning *of repolarisation can induce either auricular flutter or fibrillation.*

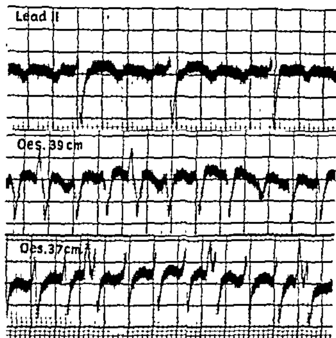


FIG. 109 Auricular flutter with 3 1 A-V block The œsophageal lead shows auricular intrinsicoid deflections which are predominantly negative at 39 cm and are separated by a well defined iso electric interval

This favours this view that each is due to multiple re-entries with many short circuses *(24)*

In auricular fibrillation simultaneous electrocardiograms taken from each auricle during valvotomy showed in 3 out of 4 patients that the rate of the right auricle was *faster than that of the left*, the average speed being 314 in the right auricle and 292 in the left *(25)*. Some of the waves resembled intrinsicoid deflections there were many irregular waves up to 0 4 mv. and small rapid oscillations

CLINICAL EVIDENCE Records taken with the œsophageal lead in auricular flutter appear to be identical with those of auricular paroxysmal tachycardia except that the rate is faster. Large regular intrinsicoid deflections are seen which are usually negative at the caudal end of the auricle suggesting an ectopic focus Although on account of their size and speed there is no steady base line between them, at levels above and below the optimal point they appear as discrete deflections separated by an iso-electric period (Fig. 109). Pressure tracings taken of episodes of flutter during catheterisation show effective contractions of the auricle corresponding to each flutter peak In one case with tricuspid stenosis giant "a" waves occurred with a magnitude of 18 mm Hg (26). The evidence in favour of a single ectopic focus is very strong. Some intracardiac ECG suggest [illegible] exist in [illegible] ent from those of flutter. Intrinsicoid deflections are seldom seen. When they occur they are quite irregular and have the characteristic waxing and waning seen with the fibrillary waves in other leads At no levels do iso-electric periods occur Yet fibrillation is closely linked to flutter. Under treatment with quinidine the fibrillary rate slows and a state of impure flutter may supervene In a series where frequent electrocardiograms were taken pure flutter was recorded in 50% and half of them passed on to normal rhythm (27) It seems possible that flutter is a normal transitional stage between fibrillation and sinus rhythm The reverse process has been observed several times (28) When the rate of discharge reaches the "fibrillation threshhold" auricular premature contractions are seen and then the irregular waves and rapid oscillations of fibrillation ensue. These tally with the fibrillar contractions observed by McWilliam in 1887 (28)

Summary. The belief that a single circus movement can account for either auricular flutter or fibrillation is now hardly tenable The evidence against it is too strong. Auricular flutter appears to be due to a single ectopic focus differing only from auricular tachycardia in the speed of the impulse formation The problem of auricular fibrillation is more complex The most likely explanation is that with increasing speed of the ectopic focus, premature beats occur which are able to re-enter the muscle giving rise to multiple small circuses. This would account for the waxing and waning quality of the fibrillary waves. But the possibility of multiple heterotopic foci cannot be excluded (29)

Auricular Fibrillation

Auricular fibrillation is a common disorder. It is found in the majority of cases of heart failure.

Ætiology. There are no histological lesions specific for fibrillation. Morbid changes are often present, but similar changes occur when the rhythm has remained normal Of the predisposing causes cardiac rheumatism, age and the influence of the vagus are important

(1) CARDIAC RHEUMATISM accounts for more than half of all cases In mitral stenosis it is almost certain that fibrillation will supervene sooner or later, unless an infective endocarditis has killed the patient first. Occasionally normal rhythm persists to the end

(2) THE ELDERLY GROUP. Auricular fibrillation is found in elderly people who show little other evidence of cardiac disease In a series of 20 cases of this type, all were men, the average rate was about 70 *(30)*

(3) VAGUS. Vagal influence is probably the underlying factor in a miscellaneous group including electric shock, acute indigestion or appendicitis, also when fibrillation occurs in digitalis poisoning.

(4) HYPERTHYROIDISM. Auricular fibrillation is a well-recognised complication of thyrotoxæmia, especially in the older patients The subject is discussed in Chapter 6

OTHER CAUSES Auricular fibrillation occurs as a rare complication in cardiac infarction (p. 264), and in pneumonia It may follow myocardial contusion due to a non-penetrating injury of the chest (p. 172). It is not uncommon after pneumonectomy for carcinoma of the lung The only congenital defect with which it occurs is in the atrial septal defect (p 55)

Diagnosis. The diagnosis of auricular fibrillation is usually quite easy. The pulse is characteristic It is totally irregular. The beats are irregular in strength and in spacing There appears to be no relation between the size of any beat and that of the preceding pause thus a small beat may follow a long interval, and a large beat succeed a short one At no time can any succession of rhythmic beats be made out. There is a complete absence of a dominant rhythm

EXAMINATION OF THE HEART When the pulse rate is very fast, the irregularity may not be easy to appreciate Auscultation at the apex may solve this difficulty, and the diagnosis should always be confirmed by auscultation. Some of the weaker contractions, failing to overcome the aortic pressure, will cause no wave to be transmitted

to the wrist They may be heard at the heart, but will not be felt at the wrist Sometimes these extra beats will make the irregularity more pronounced, though they will not always do so

If the mitral valve is normal, the first sound will vary in intensity, depending upon the interval between it and the preceding beat. The loudest sound occurs when the interval is short and the ventricle contracts during the early diastolic filling phase (*31*). The valves descend during this phase, and, as with premature systoles, will travel fast to reach the position of closure and so will vibrate strongly. If the mitral valve is diseased and incompetent this feature will be less obvious since only the tricuspid will close.

EFFECTS OF EXERCISE The irregularity of fibrillation usually becomes more pronounced on moderate acceleration of the heart. When the rate is slow, and there is any doubt as to the nature of the irregularity, the patient, if well enough, should be re-examined after moderate exercise, when the diagnosis will usually become obvious

ELECTROCARDIOGRAMS Besides the total irregularity in the spacing of the ventricular complexes, the P (auricular) waves are *absent* In place fibrillary waves are usually seen They are rapid and irregular oscillations, occurring between 350 and 500 times a minute They are often obvious at one part of a lead, and *then dis-* [illegible]

[illegible] waves, as a rule But they are always present, and in the flat curves of fibrillation in which no oscillations may be visible between the ventricular complexes, they can still be seen superimposed upon the T waves, and careful inspection will show that no two T waves are exactly the same Fibrillary waves are best seen in the œsophageal lead and in precordial leads to the right of the sternum

In curves showing fibrillation and left ventricular hypertrophy, the T waves are more deeply negative after the shorter pauses, whilst in two cases of flutter and subepicardial anterior infarct, T was more negative after the longer pause Lead V4 showed these changes best which were presumably due to alterations in the speed of repolarisation in the abnormal part of the myocardium (*32*). The Q-T time in fibrillation does not vary with the cycle length, but depends upon the average ventricular rate. If this is calculated charts can be used to determine if the Q-T is normal or not (*33*). In patients who are fully digitalised, the node may escape The

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(4) HYPERTHYROIDISM Auricular fibrillation is a well-recognised complication of thyrotoxæmia, especially in the older patients The subject is discussed in Chapter 6

OTHER CAUSES. Auricular fibrillation occurs as a rare complication in cardiac infarction (p 264), and in pneumonia It may follow myocardial contusion due to a non-penetrating injury of the chest (p. 172) It is not uncommon after pneumonectomy for carcinoma of the lung The only congenital defect with which it occurs is in the atrial septal defect (p 55).

Diagnosis. The diagnosis of auricular fibrillation is usually quite easy. The pulse is characteristic It is totally irregular The beats are irregular in strength and in spacing There appears to be no relation *between the size of any beat and that of the preceding* pause. thus a small beat may follow a long interval, and a large beat succeed a short one At no time can any succession of rhythmic beats be made out There is a complete absence of a dominant rhythm

EXAMINATION OF THE HEART When the pulse rate is very fast, the irregularity may not be easy to appreciate Auscultation at the apex may solve this difficulty, and the diagnosis should always be confirmed by auscultation Some of the weaker contractions, failing to overcome the aortic pressure, will cause no wave to be transmitted

irregular fibrillation there is an inverse relationship between this period and the length of the preceding cycle The length of mechanical systole is greater after the longer pauses, since the diastolic pressure is lower and the ventricle is better filled. The result is a large beat with a high pulse-pressure Pulse pressures, however, differ in cycles of equal length since efficiency is probably lower if any cycle is preceded by several short ones With slow fibrillation recovery takes place and there is little change in the systolic pressure with varying cycle lengths (35). Under digitalis therapy the maximum efficiency is attained when the apex and pulse rates are most nearly the same The point at which this occurs varies in different individuals, but it will not usually be reached until both rates are under 80

Exercise causes an undue acceleration of the heart in fibrillation (36) There is also a delay in the return to the resting level. The acceleration is usually due to a decrease in the vagal tone. The fibrillary waves become slower, and so a greater number of stimuli pass down the bundle.

Emotion can lead to acceleration through an increase in the conductivity of the bundle due to over-action of the sympathetic ... a tendency to ... This tendency ... n these cases sedatives should be given as well as digitalis. More placid types and elderly people ... vagal influence, can ...

... restoration of sinus rhythm showed that the output and the stroke volume increased both at rest and during exercise The oxygen content of the blood in the pulmonary artery increased resulting in a fall in the arteriovenous oxygen difference (37) The peripheral resistance fell in 9 out of 14 cases (38) The probable cause of the improvement is that the heart is better filled when the auricle contracts (39)

Prognosis. Auricular fibrillation occurs so commonly as a ...

... the ventricular muscle. The longest recorded case of persistent fibrillation, according to ...

escape beats have the same contour as the normal beats but are slower. In one series the average ventricular rate was 57, while the A-V nodal rate was about 44 (*34*).

DIFFICULTIES IN DIAGNOSIS. There are three conditions which are difficult to distinguish from fibrillation.

Multiple premature systoles, especially if they are arising from more than one focus in the heart, may give rise to an irregularity very similar to that of fibrillation. The exercise test may not assist as the rate is often already fast A combination of fibrillation and premature systoles may cause difficulty, if the rate is slow, the fibrillation may be missed.

Partial heart block with many dropped beats, when it occurs at a relatively rapid rate, may cause an arrhythmia clinically indistinguishable from fibrillation.

Auricular flutter, when the ventricular rate is slow and irregular, may be impossible to distinguish from fibrillation without an electrocardiogram.

EFFECT OF THE ONSET OF FIBRILLATION. The effect of the onset of fibrillation depends upon the previous condition of the heart, and upon the speed at which the ventricles are driven

The speed of the ventricles varies inversely with that of the fibrillary waves. A healthy auriculo-ventricular bundle will not transmit impulses above a certain rate, and the higher the rate at which it is stimulated the fewer impulses will it conduct. If other conditions are equal, more stimuli will reach the ventricles with a fibrillary rate of 350 a minute than with a rate of 500. The highest recorded ventricular rate in fibrillation is 220, but it is not often that speeds of 160 are exceeded

If conduction in the bundle is impaired, few stimuli will pass, and the onset of fibrillation may not cause any acceleration of the heart Complete heart block with a slow and regular idio-ventricular rhythm may exist with fibrillation

In *advanced mitral stenosis, the onset of the rapid and* disorderly rhythm of fibrillation usually brings on heart failure On *the other hand in elderly people the ventricular rate may* be but little affected by the fibrillation because of latent heart block, and they may be unable to remember when the arrhythmia began.

COURSE Auricular fibrillation lowers the efficiency of the heart When the ventricular rate is rapid, many beats are ineffective and not reach the pulse The electro-mechanical latent period which

the left ventricle

le. In rapid and

this type of tachycardia (*44*) The attacks may be prolonged; they cause much disability and may prove fatal (*45*). Complete dissociation has been recorded (*46*) In one series of 40 cases digitalis seems to have been a factor (*47*) Nearly all had had congestive failure before the tachycardia began and had received digitalis, frequently to excess Half of these patients died. This type would

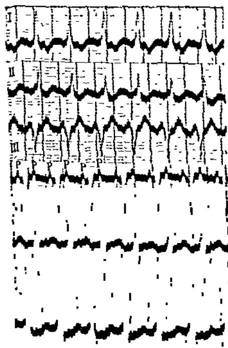


FIG 110 Auricular tachycardia with 2 1 heart block Auricular rate is 320 Ventricular rate is 160

appear to conform more nearly to modern conceptions of flutter than to auricular tachycardia, and provide further evidence that they are basically the same

Physical exam

a regular pulse of

positions, whether he

be due to auricular

The jugular pulse in the neck should be

The rapid and regular auricul

in the pulsation of the

twenty years (*40*) These cases are exceptional, however, and auricular fibrillation must be regarded as a serious incubus upon the heart. When it occurs in a heart which is already meeting the demands upon it with difficulty, failure may come on rapidly.

Auricular Flutter

Auricular flutter is an uncommon disorder, occurring in many types of heart disease. The average age of onset is somewhat later than in fibrillation, most patients being from forty to seventy, although examples have been found in infancy. Arteriosclerosis and hypertension are found in the majority of cases (*41*), but flutter may also occur in chronic rheumatic heart disease and in hyperthyroidism, occasionally it is seen in acute rheumatic carditis Paroxysms may follow cardiac infarction, or an acute infection, such as influenza, or pulmonectomy It may be associated with an atrial septal defect.

Diagnosis. Since it appears likely that auricular flutter is due to the activity of a single ectopic focus, the distinction between flutter and supraventricular tachycardia lies only in the speed at which impulses are formed in the centre But the dividing line is not clear cut In flutter, oscillations of the fibre are seen which have a sharp uprising and a more gradual fall These oscillations are called the "flutter peaks," and it is noticeable that as soon as one ends the other begins. These features are not so obvious in the œsophageal lead in which it is apparent that the large intrinsicoid deflections are not separated by a base line simply on account of their speed. The other characteristic of flutter is that the ventricle, except on very rare occasions, does not answer all the auricular beats The usual response is to answer half (1:2 response) With an average auricular frequency of about 300, the ventricle responds with a regular rate of 150 In some patients the ventricular response is slower (1:3 or 1:4 response), the rate is then less than 150 and the rhythm is *irregular*. With higher grades of block the node escapes, until finally all the beats are of nodal origin and complete A-V dissociation is present, as was present in the original case of flutter described by Ritchie (*42*)

A not uncommon group of cases possesses one but not the other of these characteristics 2:1 heart block is present, but discrete P waves take the place of the flutter peaks The auricular rate may vary from 160 to 400 (Fig. 110) Flutter peaks may be seen in some with a slower rate, and iso-electric periods in others with a faster rate ... Paroxysms of fibrillation and flutter may alternate with

1:2 FLUTTER. Usually every other stimulus is transmitted to the ventricles so that the ventricular rate is regular, and varies from 130 to 180 Sometimes a stimulus will be dropped at intervals so that at one moment every other impulse and at another every third will be transmitted. The ventricular rate will then be about 120 and slightly irregular. Some of these cases show Wenckebach periods with increasing flutter-peak-R intervals until a beat is

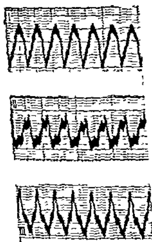


FIG 112A Auricular flutter, nearly 300 1 1 ventricular response

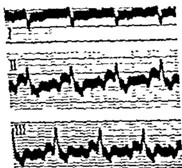


FIG 112B Auricular flutter 1 2 ventricular response From the same case as A

dropped (*51*) When every other stimulus is answered, 1.2 heart block is said to be present This does not imply that there is any disease of the conducting tissue, it is merely a method of expressing the ratio of the auricular to the ventricular rates

When the ventricular complexes are abnormal as in bundle branch block, or recent infarction the flutter peaks may be obscured, except in the œsophageal lead. Increasing the block by means of carotid sinus pressure may enable the diagnosis to be made in these cases

1.1 FLUTTER The human ventricle is not capable of maintaining rates of over 300, and speeds of over 200 are not well tolerated The lower flutter rates are among those which can just be maintained, so that every impulse may be transmitted and the ventricle will then beat at a speed of 200 or more (Figs. 112A and 112B) Attacks

and it may be possible on occasions to make out waves which are much faster than the ventricular rate, especially if pressure on the carotid sinus is effective. Occasionally in these patients the flutter sounds can be heard, and the auricular movements may cause a perceptible vibration of the chest wall. The contractions of the auricle can occasionally be seen on the screen with the patient in the right oblique position and barium in the œsophagus; the column of barium vibrates. Pressure records taken from the brachial artery sometimes show the rapid auricular waves (*48*). As in fibrillation or premature systoles the loudness of the first heart sound

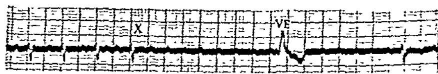


FIG. 111 Auricular flutter. Pressure carotid sinus (X) causes transient ventricular standstill. Ventricular escape (V.E.) occurs.

depends upon the position of the A-V valves when the ventricle contracts. Loud sounds were heard when the upstroke of the flutter peak came about 0 20 sec. before R (*49*)

Carotid sinus pressure may cause the ventricular rate to slow and become irregular for as long as the pressure is maintained: then the original rapid rate is resumed in steps (Fig 111) The flutter waves of the external jugular veins may be seen to persist This serves to distinguish flutter from other forms of paroxysmal tachycardia, but occasionally a sinus tachycardia responds in a somewhat similar manner. If the pulse is from 100 to 120 and irregular, mild exercise may cause it to accelerate to about 150, and to become regular

Too much reliance must not be placed on these methods of diagnosis. The carotid sinus response, when seen, is characteristic, but in most cases an electrocardiogram is required for the diagnosis.

Electrocardiograms. The flutter peaks with their sharp uprising and more gradual fall are distinctive. They are usually seen better in leads in F and so in II and III rather than in lead I They are perfectly constant in shape and time in each subject, and they have a very similar shape in different subjects, although the rate may vary considerably. The usual rate is about 300, but they have been found as low as 180 and as high as 360 a minute. In the œsophageal lead large intrinsicoid deflections are seen at the auricular levels Occasionally they may be found when no flutter peaks are visible in the other leads (*50*).

appears there may be congestion of the lungs The attacks ...

Paroxysms of tachycardia may be due to transient auricular fibrillation or flutter, to auricular paroxysmal tachycardia or to ventricular tachycardia Ventricular fibrillation is so closely associated with the last that it is also considered here

Paroxysmal auricular fibrillation. Paroxysms of fibrillation usually end spontaneously within two days Normal rhythm is not likely to return after a week, although occasionally it may do so after months or years

Paroxysms occur under three conditions A series of paroxysms may precede the onset of permanent fibrillation This is not uncommon in mitral stenosis or hyperthyroidism. It seems as though the auricular muscle has reached a state when any stimulus will be sufficient to excite fibrillation Auricular premature systoles are often present at this stage The paroxysms may last from a few beats to some hours

In another group are the isolated paroxysms They have usually a definite exciting cause, such as a coronary occlusion, or they arise during the course of an infection In the same category are the attacks due to vagal influence, such as those caused by electric shock, or following some mental disturbances

In true paroxysmal fibrillation the patient may undergo a succession of these attacks at shorter or longer intervals over a number of years Often a careful search fails to find any satisfactory cause In some cases toxic conditions, such as cholecystitis or pyelitis, are associated with the paroxysms Pressure on the left auricle from a lymphomatous nodule in the left root was the cause in one case X-ray therapy stopped the paroxysms (*54*) The attacks are not dangerous, but they may give rise to much disability Sometimes they end by the fibrillation becoming established, sometimes the condition proves amenable to treatment

Paroxysmal auricular flutter. One-quarter of all cases of auricular flutter are purely paroxysmal, and attacks are often



FIG 113 The arrow marks the end of a paroxysm of flutter The next attack starts with an auricular extra systole (E S)

have been recorded in which the ventricular rate was between 250 and 300, and several in which it was about 200, mostly occurring during the auricular slowing brought about by quinidine (52). These attacks may also be provoked by exertion. They are usually serious, and sometimes cause loss of consciousness, and they may account for some of the deaths which are classified as syncope.

SLOW VENTRICULAR RATE IN FLUTTER. When the ventricle responds sometimes to every third, and sometimes to every fourth impulse, the rhythm will be irregular and the rate will be comparatively slow. When the rate is below 120 it is probable that the bundle is diseased, although the expressions 1:3 and 1:4 heart block are again merely methods of expressing a ratio. When the rate is under 60, disease of the conducting tissue is certainly present, and complete heart block is sometimes met with in flutter

Course and prognosis. The onset of continuous flutter is a more serious event than the onset of fibrillation. Ambulant cases of flutter are not so easily controlled by digitalis, and they are liable to an abrupt doubling of the ventricular rate on exertion. A change from flutter to fibrillation is almost always beneficial to the patient; but as in fibrillation the prognosis as to life depends upon the underlying cardiac condition.

Paroxysmal Tachycardia

A paroxysm of tachycardia is a bout of rapid heart action which starts quite suddenly, has a variable duration, and ends as suddenly as it began. The rate of the ventricles varies from 120 to 300 a minute. Some patients are prostrated by the attack and have to lie down till it is over; others are but little inconvenienced The patients complain of palpitation and perhaps suffocation with a sense of fluttering in the chest The rapid beating of the heart is often distressing Precordial pain may develop. The blood pressure falls and giddiness and faintness may be caused by the defective cerebral circulation There may be acute mental disturbances such as hallucinations, and epileptiform convulsions may occur Nausea is sometimes noted Polyuria may occur (53).

The duration of a paroxysm is very variable It may only consist of a few beats, or last for days. Most paroxysms end within two days, but some have lasted for a year or more

In prolonged paroxysms the circulation is slowed and the heart may fail. This is more likely to occur if the heart was previously diseased. The patient becomes orthopnœic, and may vomit, or precordial pain may be felt Venous engorgement and cyanosis

seen in nodal tachycardia If the R-P interval is much lengthened reciprocal rhythm can occur (*60*) (see p 295) After long paroxysms the T wave may become inverted for a time, presumably due to exhaustion of the heart muscle (Fig 115).

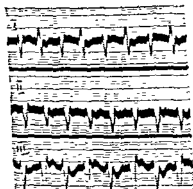


FIG 114 Nodal tachycardia at a rate of 194 with bidirectional ventricular responses (QRS, 0 09 sec)

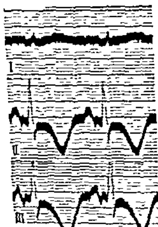


FIG. 115 Negative T waves after a long paroxysm of auricular tachycardia.

REPETITIVE TACHYCARDIA A continuous succession of short runs of auricular tachycardia occur separated by one or more normal beats (Fig 116) The combined rate varies from 90 to 150

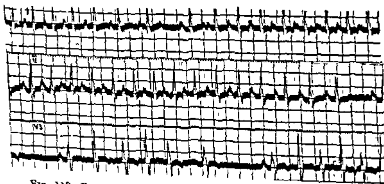


FIG 116 Repetitive auricular tachycardia at 180. Note intermissions in each lead Electrical alternation occurs at the end of V3

associated with paroxysms of fibrillation (52). Paroxysms of flutter tend to recur and become more frequent, and they easily lead to heart failure if at all prolonged.

Cases with numerous short attacks consisting of a few flutter peaks only are sometimes found (55). (Repetitive Tachycardia) (Fig. 113).

Supraventricular tachycardia comprises auricular and nodal tachycardia. The distinction is somewhat artificial and is based upon the different appearance of the P waves in the limb leads. In most attacks of auricular tachycardia, unless the beginning or end has been recorded, the P waves cannot be seen, being buried in the QRS or T waves. When present they are abnormal and usually inverted. In the comparatively rare type of nodal tachycardia inverted P waves follow the QRS. In the œsophageal lead the auricular intrinsicoid deflections are clearly ectopic and frequently resemble flutter in having predominant S at the lower levels. There is no means of distinguishing an auricular or a nodal origin of the focus.

In supraventricular tachycardia the heart beats at a rate varying from 120 to 300, but in most cases the rate is about 180. As a rule the rhythm is remarkably regular, the beats being evenly spaced to a fraction of a second Sometimes the rhythm is interrupted by ventricular premature systoles The rate is not usually influenced by posture or by emotion. Pressure on the carotid sinus will not alter the rate, although it may terminate the attack The mechanism is not under the control of the central nervous system. Auricular tachycardia is quite common In most instances no cause can be found for the attack Some occur only during pregnancy (56), or following operations on the chest (57), or as the result of contusion of the heart (58)

The ventricular complexes are usually of the normal supraventricular type Sometimes, however, the ventricular complexes show aberration during the attack and the curves, except in the œsophageal lead, will then simulate a paroxysm of ventricular tachycardia (Fig 114) Auricular and ventricular tachycardia may be present simultaneously Usually the rate of the two rhythms differs, but in one case they were the same and the diagnosis was made by the fact that after pronestyl the auricular tachycardia stopped first. In another there was a simultaneous auricular and nodal tachycardia When the auricular tachycardia stopped interference dissociation resulted with ventricular capture (59) Retrograde heart block with "reversed Wenckebach" periods may be

lengthened

the T wave may become inverted for ... exhaustion of the heart muscle (Fig 115).

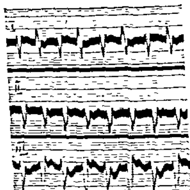


Fig 114 Nodal tachycardia at a rate of 194 with bidirectional ventricular responses (QRS, 0 09 sec)

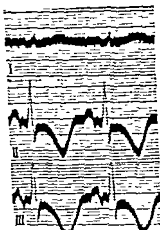


Fig 115 Negative T waves after a long paroxysm of auricular tachycardia.

REPETITIVE TACHYCARDIA A continuous succession of short runs of auricular tachycardia occur separated by one or more normal beats (Fig 116) The combined rate varies from 90 to 150



Fig 116 Repetitive auricular tachycardia at 180 Note intermissions in each lead Electrical alternation occurs at the end of V3.

2:1 heart block may be present or Wenckebach periods The prognosis is good and in most cases the tachycardia ceases spontaneously although it may persist for several years (*55*)

PROLONGED AURICULAR TACHYCARDIA. Most of the reported cases had 2:1 heart block and so perhaps should be classed as auricular flutter (Fig. 110). Thus two girls had auricular tachycardia,

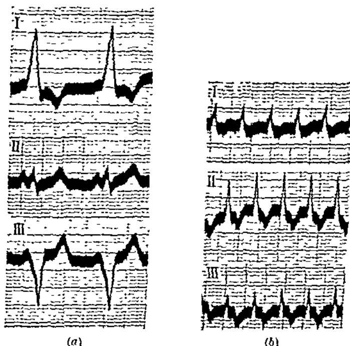


FIG 117 (*a*) Wolff-Parkinson-White syndrome. (*b*) Paroxysm of auricular tachycardia from the same case.

for six years and two years respectively, at a rate of 180 when standing, and 150 when sitting, while normal rhythm at 90 often returned when lying, 2:1 heart block being present at other times (*61*). In two more the tachycardia persisted for over eleven years but digitalis induced 2.1 block and kept the rate at about 100 (*62*). Congestive failure supervened when the rate increased to 200 (*63*), as it did in a man who had tachycardia for most of the time for more than 25 years (*64*)

AURICULAR TACHYCARDIA AND THE WOLFF-PARKINSON-WHITE SYNDROME. Paroxysms of tachycardia are not uncommon in the Wolff-Parkinson-White syndrome, and they are usually auricular in origin (*65*) (Fig. 117 (*a*) and (*b*)) During the attack the ventricular

complexes may be more normal. In other cases auricular fibrillation is present and, rarely, ventricular tachycardia (66).

AURICULAR TACHYCARDIA IN INFANCY. Paroxysms may occur in infancy with rates varying from 250 to 300 (67) The child is restless, then apathetic, and the pulse often imperceptible. Vomiting and cyanosis may occur. Fever and leucocytosis are present. Congestive failure may follow. Many of these cases have A-V heart block (68) Digitalis is the best treatment (69) (Fig 118)

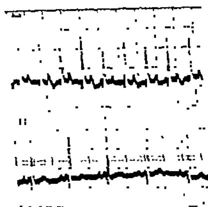


FIG 118 Auricular tachycardia in a child of 7 weeks. Ventricular rate 240 *Lower strip* shows normal rhythm after 0·2 mg Lanoxin intramuscularly in 16 hours.

Prognosis. If there is no associated heart disease, the expectation of life in auricular tachycardia does not differ from the normal In 750 cases attacks had been present on the average for 25 years, and the longest history was 64 years (70) It is impossible to predict the number of attacks any patient is likely to have The attacks may cease spontaneously, or the patient may react to treatment, but others continue unchecked Occasionally the attacks become more frequent and last longer, with more serious and sometimes fatal effects

Ventricular Tachycardia

Paroxysms of ventricular tachycardia consist of a succession of ectopic beats arising in either ventricle and having the same form as ventricular premature systoles They must be distinguished from paroxysms of auricular tachycardia with impaired conduction

2:1 heart block may be present or Wenckebach periods. The prognosis is good and in most cases the tachycardia ceases spontaneously although it may persist for several years (*55*).

PROLONGED AURICULAR-TACHYCARDIA. Most of the reported cases had 2:1 heart block and so perhaps should be classed as auricular flutter (Fig 110). Thus two girls had auricular tachycardia,

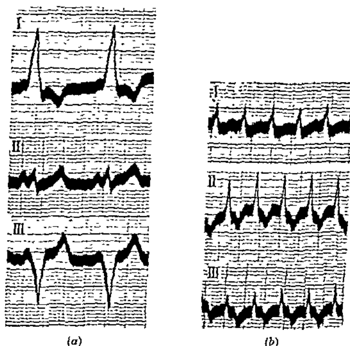


FIG 117 (*a*) Wolff Parkinson-White syndrome (*b*) Paroxysm of auricular tachycardia from the same case

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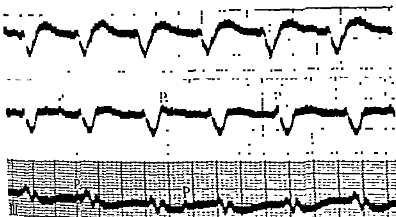


FIG. 119 Ventricular tachycardia at 110 Auricular rate at 65

FIG. 120 Simultaneous leads II and œsophageal showing termination of a long paroxysm of ventricular tachycardia. Ventricular rate 192 Auricular rate 136 No evidence of auricular activity in lead II The auricular intrinsicoid deflections are well seen in the œsophageal lead

down a bundle branch (aberration), or from auricular flutter with bundle branch block. To do so certain criteria have been established. Of these, the most reliable is the demonstration of an independent auricular rhythm with P waves occurring at a slower rate (Fig. 119) For this purpose there is no lead to equal the œsophageal in which at auricular levels the intrinsicoid deflections stand out clearly, and in many instances are actually larger than the ventricular QRS (Fig 120). *Other criteria are the presence of ventricular premature* systoles before and after the paroxysm, similar in shape to the complexes of the paroxysm, the onset of the paroxysm with an abnormal ventricular complex, and ectopic ventricular complexes occurring regularly and rapidly in auricular fibrillation (*71*). On rare occasions the œsophageal lead may show retrograde conduction to the auricle (*50*). There may be partial retrograde block, and some of the P waves may be dropped Or, when the R-P interval is long, reciprocal beats may occur, and sometimes the form of these beats is intermediate between the ventricular tachycardia complexes and sinus complexes indicating fusion beats (*72*). Fusion beats may also be due to the activation of part of the ventricle by the independent auricular rhythm and are useful evidence of a ventricular origin of the paroxysm (*73*) An auricular tachycardia may occur simultaneously with the ventricular paroxysms (*59*) (see p. 328)

Bi-directional Ventricular Tachycardia. The complexes are alternately of right and left ventricular type (Fig 121). The focus in these cases is almost certainly supraventricular, probably in the node, and the form of the ventricular complexes is due to impaired conduction down each branch of the bundle alternately. There is, in fact, an alternating bundle branch block Lesser grades may occur with alternating incomplete right and left branch block. In them the main deflections of alternate complexes have a different direction but the QRS is not widened (Fig. *114*) Carotid sinus pressure may stop the paroxysms for a time or block alternate complexes (*74*) This rare and very dangerous arrhythmia is due usually to digitalis poisoning Out of 34 cases recorded in the literature 22 were receiving digitalis (*75*)

Repetitive ventricular tachycardia is much less common than the auricular variety (*55*) One such case had hundreds of short attacks daily. Many attacks began with fusion beats (*76*)

Clinical features. The ventricular rate during the attack varies from 100 to 300. When the rate is over 240 a *Wolff-Parkinson-White syndrome* should be considered, especially if the patient is not in shock and has palpable peripheral pulses and a systolic pressure

Ætiology. Ventricular tachycardia is much less common than auricular tachycardia, and is found under three conditions In about one-tenth of the cases the heart is otherwise normal (*81*). These include patients with repetitive ventricular tachycardia and the Wolff-Parkinson-White syndrome Attacks may continue for years and then cease (*82*) One such case had numerous paroxysms when he was tense and unhappy (*83*) They are usually easily controlled by quinidine In this category also are the short paroxysms which are frequently induced during cardiac catheterisation, when the tip is in contact with the right ventricular wall They may also occur with the catheter in other positions such as in the right auricle or pulmonary artery and are then probably reflex in origin (*84*) Withdrawal of the catheter nearly always brings them to an end, but occasionally a paroxysm may continue for hours (*85*). Short paroxysms of ventricular tachycardia have occurred at the end of the forced expiration of the Valsalva manœuvre performed to stop an auricular tachycardia They may have been due to the release of adrenaline (*86*)

In the great majority of cases severe disease of the heart muscle is present, usually cardiac infarction involving the septum. In 44 out of 100 patients the attack followed infarction (*87*). Full doses of digitalis was a factor in some but digitalis is not so prone to cause ventricular tachycardia after infarction as was formerly thought In fact, digitalis has been given intravenously during attacks without untoward results (*87*) Ventricular tachycardia has *followed an* exercise test in a patient with angina pectoris (*88*) Bi-directional ventricular tachycardia is due to digitalis intoxication but only in the presence of myocardial disease. It cannot be produced experimentally, *nor does it* occur in cases of suicide with digitalis

In the presence of A-V heart block, ventricular tachycardia may be the precursor of ventricular fibrillation which is one of the causes of Stokes-Adams' attacks (see p 292)

Prognosis. As might be expected the prognosis in cases with myocardial disease is bad Most patients have died either ... hou...

... type the immediate prognosis is extremely grave Unless the cause, such as *digitalis*, can be stopped at once, the patient is likely to die within twenty-four h... ...

of more than 100 mm. Hg. It seems that in this condition the irritable nodal and bundle fibres can conduct the impulse at supranormal speeds (*77*). Attacks may last from a few beats to two months (*78*) In prolonged attacks shock is severe and they usually end fatally. In those that recover, the prolonged state of shock can cause a lower nephron nephrosis with vomiting and raised blood urea (*79*). The

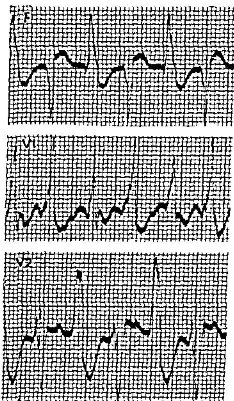


FIG. 121. Bi-directional ventricular tachycardia.

rhythm is usually regular, but sometimes there are slight variations in speed which may be perceptible clinically The first sound at the apex is widely "split" In the presence of an independent auricular rhythm the sounds may vary slightly in intensity owing to alterations in the position of the A-V valves when the ventricles contract, as in premature systoles. Also giant "a" waves can be seen at irregular intervals in the jugular veins, due to the right auricle contracting against a closed tricuspid valve They tend to vary in strength as the tricuspid may be partially open (*80*) Carotid sinus pressure has no effect upon the tachycardia

which the size of the complexes is diminished If they last 30 sec. consciousness is lost.

The fully developed attack of ventricular fibrillation lasts up to six minutes Incoordinate contractions occur with a frequency of 240-380 (Fig 123) The oscillations in the electrocardiogram vary

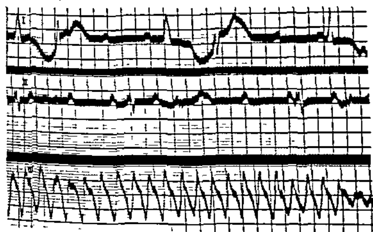


FIG 122 Ventricular fibrillation Prefibrillary phase Lead I Abnormal ventricular complexes with grossly deformed T waves and premature systoles on their ascending limb. Lead II Complete heart block Lead III Ventricular "flutter" Regular ventricular rhythm at 270.

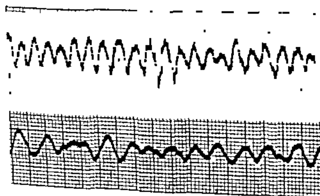


FIG 123 Ventricular fibrillation *Upper strip* Undulatory phase Ventricular rate 380 *Lower strip* Terminal phase showing broadening of QRS

ventricular tachycardia has the worst prognosis of any of the cardiac arrhythmias.

THEORIES OF CAUSATION. An *ectopic ventricular focus* probably accounts for paroxysms occurring in structurally normal hearts It is possible that the focus may be in the node or the bundle, and that the form of the ventricular complexes may be due to aberration owing to their prematurity This is almost certainly the case in the bi-directional type

Re-entry is a likely cause in paroxysms following infarction or when there is disease of the conducting tissue, auriculo-ventricular or bundle branch block. A normal ventricular premature systole spreads rapidly, and all the ventricular muscle is refractory at the same time. If conduction is defective, the spread might be uneven, owing to the increased refractoriness of some areas, and re-entry might occur. Ventricular tachycardia may thus be due to circus movement and be closely linked to ventricular fibrillation.

Ventricular Fibrillation

Ventricular fibrillation can occur spontaneously or during cardiac surgery, or as the result of certain diagnostic procedures.

Spontaneous ventricular fibrillation is one cause of Stokes-Adams' *attacks* When *the ventricles fibrillate* the *pulse* at the wrist ceases, contractions cannot be heard at the heart and the patient becomes unconscious (see p 293)

Ventricular fibrillation is preceded by several definite stages (89) If the rhythm is normal, simple acceleration may occur or several pace-makers may appear, or ventricular premature systoles may be seen. If A-V dissociation is present, there may be a simple acceleration of the idio-ventricular rate, and the faster rate may alternate with the previous slow rate When the idio-ventricular rate reaches 50, ventricular premature systoles occur, which have the same shape as the basic ventricular complexes Ventricular complexes with massive inversion of the T wave are seen with the premature beat on the ascending limb (Fig 122) Interpolated ventricular premature systoles may cause a sudden acceleration to 120, or else there may be short runs of ventricular tachycardia Ventricular premature systoles from a constant focus invariably precede fibrillation, the onset of which seems to be facilitated by the gradual acceleration.

During the initial fibrillary period which also may last from some minutes to days, short bursts of ventricular fibrillation are seen in

days he had an acute tubular nephritis, with hypertension, raised blood urea, albumen and casts (*95*).

THEORY OF CAUSATION. Ventricular fibrillation may supervene in many experimental procedures upon the heart. Attacks can be induced by a single strong electric shock during the critical period in late systole. Cooling the ventricle in dogs when sinus rhythm is present causes only ventricular premature systoles, but if performed during auricular flutter or fibrillation induces ventricular fibrillation (*96*). It seems probable that *re-entry* takes place, leading to multiple small "circuses." On this is based the treatment of electric defibrillation in which serial small shocks are administered (see p. 294).

Treatment

GENERAL CONSIDERATIONS. In the auricular arrhythmias, and especially in auricular fibrillation, treatment may aim at controlling the rate and thereby increasing the strength of the ventricular contraction. This is effected by means of digitalis (see p. 321). When digoxin was introduced through a cardiac catheter in patients with uncontrolled fibrillation the cardiac output rose and the right auricular pressures fell in most of those who had congestive failure, and there was an increase in the excretion of salt. When congestive failure was not present, there was but little change (*97*). Normal rhythm may return after digitalis therapy in auricular fibrillation, especially if congestive failure has been present, but this follows the general improvement in the circulation and is not due to any specific effect upon the auricles. In flutter, however, and in auricular tachycardia in infants, digitalis may be the best means of restoring normal rhythm. Quinidine may be employed in selected cases of fibrillation. In auricular tachycardia vagal stimulation and, in particular, carotid sinus pressure may terminate the attack. In the ventricular arrhythmias digitalis is useless and may be dangerous, and quinidine or procaine amide are the only effective remedies.

Quinidine is a general cardiac depressant, and causes both pulse rate and blood pressure to fall. In rare cases who die from quinidine shock, bradycardia is marked and the patient may be pulseless (*98*). The systolic blood pressure may fall 60 mm. after a single large oral dose (*99*). When large doses are employed the blood pressure should be taken after each dose and quinidine stopped if the diastolic pressure falls by 20 mm. Hg (*100*).

Quinidine depresses conduction in the ventricles. With large doses the QRS widens. Caution should be exercised if the widening exceeds 25% and quinidine should be stopped if it reaches 50%.

also in amplitude, and they may change abruptly to regular and equal complexes at a rate of 130–170, and then revert to incoordination. With asphyxia the rate may fall to 90, and the oscillations may be only 2 mm. in amplitude Though the blood pressure falls, there is always some force of pulsatile activity, and the arterial *curves bear no relation to the electrocardiograms.*

After the attack there is a post-undulatory pause or cardiac standstill which may last up to a minute The auricles cease beating after 10 sec. Short pauses are *followed by an immediate return* to the basic rhythm, and this may give place to ventricular tachycardia and then to another attack Prolonged asystole may be followed by several shorter periods, and then slow aberrant ventricular complexes.

PRECIPITATING CAUSES. Ventricular fibrillation is a recognised risk in complete heart block especially if bundle branch block complexes are also present. It has been recorded during the course of infarction. The patient recovered but had complete amnesia of the attack *(90)* The rapidly acting glycoside, acetyl strophanthidine, caused *death from ventricular fibrillation* in a few minutes when given intravenously *(91, 92)*. Attacks of ventricular fibrillation have been precipitated by injections of adrenaline given for Stokes-Adams' disease, assumed to be due *to ventricular standstill* The rare instances of sudden death after intravenous mercurials, quinidine or procaine amide, are probably due to ventricular fibrillation as is that due to diodone given for angiocardiography Hypoxia combined with loss of potassium seemed to be the cause in a psychotic emphysematous man with hypokalæmia from massive daily doses of Epsom salts, who was given morphia and developed an ineffective cough Recovery took place after an airway had been secured by tracheotomy *(93)*. Although the arrhythmia is usually terminal, some patients have numerous attacks over a number of years

Ventricular fibrillation during cardiac surgery. Ventricular fibrillation is a major hazard in extensive or prolonged operations on the heart The chief causes are general anoxia from the anæsthetic, temporary acute obstruction to the circulation, sudden hæmorrhage from the heart, coronary air embolus via a pulmonary vein or an atrial septal defect, or any operation on the left side of the heart, unless the aortic valve is kept closed *(94)*. The immediate treatment is cardiac massage through *an incision in the 4th and 5th intercostal* spaces in order to maintain a blood supply to the brain. By this means one patient made a complete recovery *after nearly two hours* of continuous *ventricular* fibrillation, although for the next few

intervals The apex rate is charted hourly to note if normal rhythm returns, or if undue acceleration occurs. In either case quinidine is stopped. The pulse is often found to have become regular when the patient wakes next morning If it has not done so, the same quantity of quinidine is repeated on the second day. On the third day 10 gr are given as the last dose On the fourth day three doses of 10 gr. are given (*109*). If the fibrillation is still refractory, digitalis is substituted until the apex rate has been brought down to below 80 It is then stopped and the course of quinidine is repeated If the fibrillation still persists, the attempt to restore normal rhythm is given up, but more than two-thirds of all cases will respond at some time during the course

If the serum levels are being measured, larger doses can be used: five doses of 0 2 g (3 gr.) can be given at intervals of two hours on the first day, and the dose doubled on the second On the third day a further 0 2 g is added to each dose. The dosage is not increased beyond that unless the serum levels are below 8 0 mg. and there are no signs of toxicity such as bundle branch block, ventricular premature systoles, hypotension, vomiting or diarrhœa (*106*) If these are absent, the dosage can be increased by further increments of 0.2 g to a limit of 1·2 g Four-fifths of conversions take place at levels up to 8 0 mg , the average being 6 mg (*110*) When the total daily dose exceeds 3 g , several electrocardiograms should be taken during the day, including one before the last dose The serum level should be obtained two hours after this dose

INTRAVENOUS QUINIDINE should be reserved for emergencies, such as ventricular tachycardia, as it is not free from risk. The best preparation is the quinidine dihydrochloride which is soluble in 1–4, 3 gr. are made up in a 2 ml ampoule Up to 10 gr can be given at a time if necessary It is safer to give the injection under electrocardiographic control so that it can be stopped as soon as the arrhythmia ceases Other preparations used are quinidine sulphate dissolved in propyline glycol (*111*)—quinidine lactate 0 65 g in 10 ml ampoules (*112*), or quinidine gluconate 0 65 g. in 20 ml (*113*) Quinidine gluconate 0 8 g in 10 ml can also be given intramuscularly (*106*)

Maintenance dose After the restoration of normal rhythm it is usually advisable for the patient to remain in bed a further week to avoid relapse Unless the cause of the fibrillation has been eliminated, as in thyrotoxic cases after
be given
patient is

Quinidine does not cause the Q-T time to increase; but the S-T interval is depressed in the left ventricular surface leads and the U wave is more prominent leadin

... auricular fibrillation. ... patients were receiving digitalis, and most had congestive failure which is usually considered a contra-indication (*102*) In another, with multiple valve lesions and congestive failure and also on digitalis, ventricular fibrillation resulted (*103*). The development of premature ventricular systoles is a sign to stop the drug

Toxic and allergic reactions. Tinnitus and headache are common with large doses. Vomiting and diarrhœa sometimes occur. Fever with thrombocytopenic purpura and fever accompanied by a maculo-papular rash have been reco...

SERUM LEVELS. ... was made when the ... in the serum could be estimated by the photo-electric fluorometer. After a single dose the peak level is obtained in about two hours Following 0 6 g by mouth the average peak level was 3 2 mg. per litre in one series (*105*) and 5 4 mg. in another (*106*) After 10 gr. (0 65 g) the highest figure was 5 mg (*107*). When 0·4 g was given four times daily for two days there was still 2 mg per litre in the serum twenty-four hours later and 0·39 mg after two days in those with congestive failure In normal subjects and in those with hepatic or renal disease the figures were approximately half the above at each period (*108*) Quinidine has, therefore, a cumulative action, and a patient who has a repetition of the course upon the second day will both begin and end with higher levels than on the first day Cumulation continues for three days after which the level ... steady unless the dose is ... r intravenous

...ADMINISTRATION *Oral.* Quinidine sulphate is made up in tablets containing 5 gr. or 0 2 g (3 gr) The drug is usually given by mouth when it is desired to restore normal rhythm in cases of auricular fibrillation The following scheme is safe and effective when serum levels are not available, though many other methods have been used, and some prefer to give digitalis as a routine before ... the ventricular

... grains are given, divided into six doses at two-hourly

find no tissue responsive and that possibly they may depress the activity of an ectopic focus directly.

Quinidine is four times stronger than procaine amide 24 gr. of quinidine daily were equally effective in abolishing ventricular premature systoles as 6.0 g. of procaine amide. There is no additional effect when they are used in combination (*127*). It appears that procaine amide is not more effective nor safer than quinidine (*125*)

Benadryl is similar in composition to procaine amide but needs to be given intravenously in doses of 100–300 mg. Nearly every case of recent fibrillation was converted by it, but the drug does not seem to offer any advantage over quinidine or procaine amide (*129*).

Treatment of auricular fibrillation. Quinidine is the drug of choice Although procaine amide will succeed in a proportion of cases (*122*) it is not so effective as quinidine.

When electrocardiographic control is used, it is found that most patients pass through a stage of auricular flutter before normal rhythm returns 54% did so in one series, and a further 16% remained in flutter (*130*). Probably more still would be found to do so if more frequent electrocardiograms were taken. It is mainly to prevent a possible 1:1 response during the flutter stage that digitalisation prior to quinidine is advocated. This response is, however, very seldom seen in practice, but the flutter stage during the quinidine treatment of fibrillation emphasises the close relationship between the two arrhythmias

Selection of cases Quinidine should always be given to patients with otherwise normal hearts who develop fibrillation It is also most useful in thyrotoxic cases in whom normal rhythm has not returned spontaneously after thyroidectomy or after a course of thiouracil Almost all these cases will respond

The impetus provided by the ability to measure the amount of quinidine in the blood and so to control dosage more exactly has led to the more full use of quinidine than was formerly thought permissible In one series of 115 cases of auricular fibrillation all had congestive failure and received digitalis throughout the course, two-thirds were converted (*27*) Quinidine is also recommended in mitral stenosis if the onset of fibrillation has led to a sudden deterioration. Maintenance doses of about 0.4 g. four times daily may be needed permanently (*106*) This treatment is not free from risk as 10 out of 20 deaths from quinidine occurred in patients with mitral stenosis (*131*) Other indications are the persistence of fibrillation after mitral valvotomy (*110*) and a history of previous

Procaine amide is also a cardiac depressant. Prolongation of the QRS is common with large doses. If the prolongation reaches 0·12 sec. the drug must be stopped (*114*) Hypotension occurs in 30% after intravenous dosage (*115*). When 1 g. was injected during cardiac catheterisation, the cardiac output fell, as well as the pulmonary and radial systolic pressures. The velocity of the blood flow was slowed (*116*). The accidental administration by mouth of 5·0 g., or ten times the normal dose, caused numbness, blurred vision and dizziness. The duration of QRS increased to 0·19 sec. All these cleared up without treatment in 8 hours (*117*) *Allergic reactions* in the form of giant urticaria have been noted after oral procaine amide (*118*).

Intravenous procaine amide has caused ventricular tachycardia when given to abolish auricular fibrillation (*119*), and ventricular standstill resulted when it was given to stop ventricular tachycardia in cases of infarction (*120*). Nodal rhythm and later auricular fibrillation followed the oral administration of the drug in an attempt to abolish ventricular premature systoles (*121*)

Methods of administration Procaine amide is absorbed from the gastro-intestinal tract. The peak concentration in the blood occurs in from one to two hours after an oral dose The drug is excreted slowly by the kidneys, the levels in the plasma falling by about 15% an hour A plateau level is reached after about 48 hours of repeated doses by mouth (*115*) The usual method is to give 1 g four-hourly up to five doses. With higher doses toxic effects such as nausea, vomiting, sweating and prostration are apt to appear (*122*) Another method is to begin with 0·5 g two-hourly for five doses and increase by 0 25 g to 1 or 1·5 g (*123*) Intravenously the drug is usually given at the rate of 100 mg. a minute until normal rhythm returns or toxic symptoms occur An average dose required is 300 mg. (*124*) When the dose approaches 1 g signs of toxicity such as hypotension or increase in duration of the QRS are indications to stop the injection (*125*) 50 mg a minute may be safer as 100 mg has produced ventricular tachycardia (*119*). Procaine amide has been given intramuscularly in doses of from 0·1 to 2·5 g There were no local reactions but the method does not appear to have any advantage over the other routes (*126*)

ACTION OF QUINIDINE AND PROCAINE AMIDE It was formerly thought that these drugs acted by increasing the refractory period and so slowing the circus movement until it broke Now that a single circus appears to be unlikely in any of the arrhythmias it must be presumed that they slow conduction until re-entry waves

been better in both of these cases. Flutter peaks were seen after intravenous procaine amide in cases associated with bundle branch block, [illegible]

restored normal rhythm in a young man who had paroxysms of flutter and fibrillation (*135*)

1:1 *Flutter.* Carotid sinus pressure should be used to change the response quickly to a slower rate but this effect may only be transient (see Fig 111) Since these attacks are related to exertion and may be dangerous, the patient should be put to bed, and given intravenous digitalis.

Auricular tachycardia. Many patients learn how to stop attacks Most of the methods employed cause a rise in venous pressure The Valsalva experiment, in which the glottis is shut against forced expiration, is the most effective Other methods include putting the head between the knees and pressing the thighs against the abdomen If these fail, carotid sinus pressure should be applied Pressure on the eyeballs is said to succeed occasionally when carotid sinus pressure has failed, by reflex vagal stimulation.

***The carotid* sinus.** The carotid sinus in man is an enlargement of the internal carotid artery, just above the bifurcation of the common carotid It may extend also to the adjacent part of the common carotid. The structure is derived from arteries of the third branchial arch Here the wall of the vessel is thinner than elsewhere. [illegible]
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CAROTID SINUS PRESSURE. Pressure on the carotid sinus causes slowing of the heart through the vagus In most cases there is also a fall in blood pressure. The fall is greater in hypertension and may reach 50 mm. Hg or more Both the cardiac slowing and the fall in blood pressure are more easily elicited in older patients who may react to the slightest touch Often one side is more sensitive than the other A tortuous dilated vessel may be very susceptible

Occasionally syncope may occur without cardiac slowing or a fall in blood pressure Hyperpnœa follows prolonged pressure in almost everyone regardless of whether they show the usual changes This is probably an associated reaction due to interference with the blood supply through the carotid body which is compressed at the same time.

arterial embolism. In one series of 115 cases of whom 76% were converted, 25 had had previous emboli Two only had emboli after quinidine therapy *(132)* The average level in the plasma at the time of conversion was 10 6 mg. A course of anti-coagulant therapy should be given for a fortnight prior to quinidine in these cases *(100)*.

Contra-indications. Patients in complete heart block should not receive quinidine *(106)* nor those with active infections, or gross cardiac-enlargement. Patients with rheumatic heart disease other than mitral stenosis do not usually respond *(110)*. Elderly patients *who have no symptoms from the fibrillation do not need quinidine.*

TREATMENT OF PAROXYSMAL FIBRILLATION. Intravenous quinidine dihydrochloride (3 gr.), or intravenous procaine amide (0·2–0·5 g.) may stop the paroxysm at once. Otherwise the patient *should be given a sedative such as omnopon,* ⅓ *gr , and 10 gr* of quinidine sulphate. Quinidine (5 gr.) should be repeated every two hours till the attack is over.

To prevent paroxysms, quinidine sulphate is often effective in doses of 15–20 gr. daily Moderate doses of digitalis are sometimes effective as a prophylactic. Some aim at inducing permanent fibrillation by full doses of digitalis

TREATMENT OF AURICULAR FLUTTER *Digitalis* This is the most satisfactory method Full doses should be used As the ventricular rate slows under the drug the rhythm will become irregular, although occasionally it may pass straight to a 1:4 rhythm. When it has *come down to below 80 a careful watch is kept In about 30%* of cases the rhythm will become completely irregular, since the flutter will have turned into fibrillation If digitalis is now stopped, normal rhythm may return spontaneously If it does not, quinidine may be tried *Out of 30 cases of persistent flutter half were converted* and 8 changed to fibrillation *(133)*

Quinidine is sometimes effective in removing flutter, but is seldom used As in fibrillation, quinidine slows the auricular rate, and when it has fallen to 200 a minute, or less, the ventricles may answer every stimulus. This 1 : 1 response is a reaction to be avoided Quinidine should be reserved for those cases who have not responded to a thorough course of digitalis, and digitalis must be continued while quinidine is being given Even so two patients developed a 1 : 1 response *(134)* Procaine amide is useless in flutter *(122)* A case of flutter occurring during infarction was given intravenous procaine amide. The systolic pressure fell to 60 mm. *(135)* Another received quinidine and had a 1 : 1 response *(136)* Digitalis would have

Digitalis given intravenously sometimes stops attacks, but should only be used if a ventricular origin of the tachycardia can be excluded Some prefer it to other remedies (53) In paroxysms occurring in infancy digitalis by mouth in doses up to 0·8 mg daily will stop attacks (69) Since 2:1 A-V block is easily induced, these cases are probably akin to auricular flutter in which digitalis is the drug of choice

Methoxamine is a potent pressor agent. With sinus rhythm it causes a bradycardia which is abolished by atropine (*139*). In auricular tachycardia the drug stimulates the vagus through the carotid sinus on account of the sudden rise in blood pressure (*140*) It can be given either intramuscularly or intravenously in doses of 10–20 mg. (*141*), and is useful in cases where the paroxysm has caused collapse with a low blood pressure In one case quinidine had caused vaso-motor collapse with a systolic pressure of 30 mg 20 *mg* methoxamine intravenously raised the pressure to 80 mg systolic and stopped the attack. In another, where the pressure was normal, a temporary hypertension of 220-100 was caused (*139*) In another, short runs of ventricular tachycardia occurred before normal rhythm returned (*140*)

Magnesium sulphate in doses of 20 ml of 20% solution intravenously has stopped paroxysms of both auricular and ventricular tachycardia (*142*) The effect was immediate Patients complained of a sensation of intense heat, sweating, nausea and dizziness. *Akbrin* in doses of 0 1–0 5 g intravenously has stopped a few attacks (*143*)

Auricular tachycardia with A-V block These patients have usually had full doses of digitalis and have lost potassium in the diuresis due to mercurial drugs given for congestive failure Potassium chloride in doses of 1 5–7 5 g by mouth stopped attacks in 6 cases (*111*) The effect began in 15 minutes with an increase in the ventricular rate to about 160 when normal rhythm returned, and the rate then fell gradually to about 100 In two patients with uræmia, who were taking digitalis, potassium was extracted from the blood by dialysis and they developed auricular tachycardia, the sequence of events being in the reverse order to th[illegible] up This treatment

is [illegible]

are [illegible] of doses above 3 gr

focus, or errors in diet may [illegible]

of the focus, or rectification

such as bromide or phenob[illegible]

Congestive failure increases the sensitivity of the carotid sinus reflex: so does digitalis in full doses

Electrocardiograms taken during carotid sinus compression show inhibition of the sinu-auricular pace-maker. The ventricles may beat to a slow nodal rhythm, the P waves being absent (Fig. 111). Or there may be standstill of the whole heart.

Technique of compression. The patient may be sitting or lying If lying, the head should be slightly extended and the face turned a little to the opposite side. The ampullary dilatation of the carotid should be located just below the point at which the vessel disappears under the angle of the jaw. The sinus should then be pressed firmly, or massaged up and down by the palmar surface of the thumb if the patient is lying; if he is sitting, the operator stands behind him and uses his fingers. One side should be pressed at a time, the right side first. The pressure is maintained for about half a minute, unless the heart rate reacts Both sides may be tried at once, if either fails alone.

Carotid sinus pressure may terminate an attack of auricular tachycardia. *In auricular flutter, the ventricular rate is slowed during the time that the pressure is maintained*, on release of pressure the original rate returns (Fig 111) This serves to distinguish doubtful cases. Carotid sinus pressure has no effect upon ventricular tachycardia. The pressure may cause abrupt slowing in normal sinus tachycardia, although usually it has no effect.

Vagal stimulation can also be brought about by ipecac. One or *two drachms of the syrup can be given and repeated in forty-five* minutes if the patient has not vomited or the attack has not stopped Treatment is quite safe though somewhat unpleasant Mecholyl (acetyl B methyl choline chloride) in doses of 5–10 mg given subcutaneously stimulates the vagus directly It is sometimes efficacious in auricular tachycardia, but undesirable reactions are apt to occur. These take the form of marked bradycardia with concomitant shock *The pulse may fall to 20 and consciousness may* be lost. It should not be given into a vein

PROCAINE AMIDE given intravenously is probably the best remedy for auricular tachycardia Most cases can be stopped by doses up to 500 mg. delivered at a rate of 100 mg. a minute (*114, 124*). Oral administration has also been found to be useful (*122*), but the varying duration of attacks makes it hard to gauge the effect

QUINIDINE *DIHYDROCHLORIDE, 3 gr injected intravenously*, is also very effective and prompt. The attack may end before the needle is withdrawn.

Digitalis given intravenously sometimes stops attacks, but should only be used if a ventricular origin of the tachycardia can be excluded. Some prefer it to other remedies (53). In paroxysms occurring in infancy digitalis by mouth in doses up to 0.8 mg. daily will stop attacks (69). Since 2:1 A-V block is easily induced, these cases are probably akin to auricular flutter in which digitalis is the drug of choice.

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Auricular tachycardia with A-V block. These patients have usually had full doses of digitalis and have lost potassium in the diuresis due to mercurial drugs given for congestive failure. Potassium chloride in doses of 1.5–7.5 g. by mouth stopped attacks in 6 cases (*144*). The effect began in 15 minutes with an increase in the ventricular rate to about 160 when normal rhythm returned, and the rate then fell gradually to about 100. In two patients with uræmia who were taking digitalis, —'
by dialysis and they devel
of events being in the rever
is only useful if digitalis sa ... ation is present. If doses above 3 gr. are needed, there is a risk of potassium poisoning.

PROPHYLACTIC TREATMENT. As with premature systoles, a septic focus, or errors in diet may be the cause of the attacks. Elimination of the focus, or rectification of the diet may bring relief. A sedative such as bromide or phenobarbitone is worth trying, particularly in

emotional patients. A course of quinidine, from 15 to 20 gr. daily, may be effective. Later, the dose can be reduced, and finally the drug can sometimes be discontinued

Some cases are quite resistant, and nothing seems of any use either in preventing attacks or in relieving them.

VENTRICULAR PREMATURE SYSTOLES. Unless due to digitalis *intoxication, these can be abolished almost infallibly by intravenous* procaine amide (*145*), but they soon return. Oral administration is effective in about 50% (*146*).

Ventricular premature systoles which are due to digitalis can usually be abolished for 4–22 hours by potassium chloride given in 20% solution in syrup of orange. The dose is 2–10 g. but the higher doses are apt to cause vomiting (*147*)

Ventricular tachycardia. The most effective remedy for this dangerous arrhythmia is intravenous quinidine We have used *quinidine dihydrochloride* with success in several cases and without mishap. The injection should be given preferably under electrocardiographic control, and continued until normal rhythm returns. 9 gr. (0 6 g.) has been the largest dose required This has been the experience of others (*148*) On the other hand some cases are resistant and one, having had a succession of attacks stopped by quinidine hydrochloride, required finally 3·2 g. which rendered the patient unconscious and lead to urinary suppression for two days (*78*) Intravenous *procaine amide* in doses of 0 25–0·6 g is also successful in many cases (*146*) One patient had fourteen attacks terminated *by injections of 0 5 g Normal rhythm was then maintained by* 6 0 g. daily by mouth (*149*) Large doses may be required. 1,500 mg. (1·5 g) were given at a rate of 400 mg a minute in one case. This caused the blood pressure to fall to 65 mm. and the patient became disorientated (*150*). Alternate injections of 50 mg of quinidine gluconate and of 50 mg of procaine amide at one-minute intervals *were tried in another case 1·5 g of each were needed* before normal rhythm returned after one hour (*151*). Procaine amide is recommended for the pseudoventricular tachycardias with very fast *ventricular rates which may occur in the Wolff-Parkinson-White* syndrome (*77*) Atropine (1·2 mg. intravenously) changed multifocal ventricular tachycardia occurring during catheterisation to flutter after quinidine dihydrochloride and procaine amide had failed (*85*). Isopropyl norepinephrine, 8 mg subcutaneously, stopped one attack in five minutes after procaine amide had failed (*152*). Repetitive ventricular tachycardia was controlled easily with oral quinidine (*76*).

Bi-directional Ventricular Tachycardia. Digitalis must be opped at once as overdosage with the drug is nearly always a cause f this arrhythmia. Carotid sinus pressure will block alternate com-lexes but the effect is only transitory (*74*). Potassium chloride is he most effective treatment and may be given *either by drip*

ligitalis resumed without causing tachycardia

Ventricular fibrillation. Spontaneous. Both quinidine and procaine amide are contra-indicated since complete auriculo-ventricular dissociation is present. Quinidine caused attacks in

mental confusion ephedrine was substituted in doses *of half a grain* every three hours and no more attacks occurred (*155*)

During Cardiac Surgery Cardiac massage must be started at once If more than four minutes is allowed to elapse, death will take place from cerebral anoxia (*95*) Unless the heart is already exposed, an incision should be made through the fourth or fifth left intercostal space (*156*)

One patient

The lungs a

fibrillation consist of the injection of 5 ml of 1% procaine hydrochloride, followed by 5 ml of 1–10,000 adrenaline Electric counter-shock defibrillation may be attempted by administering a succession of short shocks of 0 15–4 ampères This succeeded in 6 out of 14 episodes (*94*) If fibrillation occurs during anæsthesia, surface electrodes can be placed a few inches apart near the cardiac apex (*157*) This procedure was successful also *in one* case of spontaneous ventricular fibrillation The coronary flow can be improved by tilting the table head downwards, and by aortic transfusion Although these measures succeed in a proportion of cases, ventricular fibrillation remains a serious hazard in cardiac surgery

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CHAPTER 10

HEART FAILURE AND ITS TREATMENT

Introduction

When failure of the heart causes the circulation of the blood to be insufficient for the needs of the body, certain physiological derangements become apparent. As some of these are associated with an abnormal accumulation of blood in certain stretches of the circulation, the expression "congestive heart failure" has become widely popular But it only draws attention to one group of phenomena. It stresses the state of the blood behind the defaulting chambers, and so the terms "back pressure" and "backward failure" were introduced These date back to James Hope, in the 1830 epoch, but they came into his mind in connection with the special circumstances of mitral stenosis where there is an obstruction to the flow of blood The notions of "forward failure" came in much later, and concern the output of the heart and the rate of the circulation That these two groups of phenomena are closely interdependent is really obvious, when one recollects the words of Harvey, "that the blood moves as it were in a circle", a circle which is one indivisible physiological whole It was the work of Starling which enunciated the Law of the Heart, that laid the firm experimental basis on which modern ideas have been founded, and the foundations have not been shaken

There are four primary topics for consideration These are the effect of heart failure on

1 The output of the heart
2 The venous pressure
3 The volume of the blood
4 The rate of the circulation

Secondary topics are the effects [illegible] function, on the [illegible] lowering of the v[illegible] Cyanosis is due t[illegible] causes The liver stasis introduces important considerations

The clinical phenomena of the two types of heart failure, left- and right-sided, need special attention.

Treatment is sometimes considered directly with the object of its therapy when it has seemed convenient; sometimes a more general approach is easier, or the discussion of some special measure is more clear.

PRIMARY EFFECTS OF HEART FAILURE

Cardiac Output. This is a measure of the work the heart does In the study of heart failure the estimation of output is of fundamental importance. *The Fick principle (1870).* If the amount of oxygen is known which is needed to turn a litre of venous into arterial blood (the arteriovenous oxygen difference), then the amount of oxygen consumed in the lungs per minute divided by this figure will give the output per minute of the right ventricle That of the left ventricle can be assumed to be the same. The minute output divided by the number of beats per minute gives the stroke volume

The consumption of oxygen can well be measured by analysing samples of expired air, collected in a Douglas bag. The cardiac catheter has made the older methods of gas inhalation, ethyl iodide and so on, out of date The arteriovenous oxygen difference is easily obtained by comparing blood got by arterial puncture with samples of mixed blood from the right ventricle or pulmonary artery. It must be remembered that duplicate samples of blood from the right auricle may differ a good deal, as the different streams of blood may not mix completely Errors may also arise in the measurement of [illegible] ired air.

[illegible] give some indication of the output.

[illegible] ontraction is measured on a graph The results for the output agree fairly well with those got by other methods Dye dilution curves may also give the output.

CARDIAC OUTPUT IN HEALTH The average normal cardiac output at rest is about four litres per minute standing, and five litres recumbent. Anxiety may raise the output to ten or more litres per minute. Calm and relaxation are therefore important During exercise the output may increase to twenty-five or more litres per minute (*1*).

The output varies of course with the size of the individual The cardiac index allows for this, for it gives the output in litres per minute for each square metre of the body surface. The normal figure for this index is 3·1 litres.

When there is heart disease the output at rest is maintained at

levels until failure comes on When there is gross venous ...ion the output is about three litres a minute (2)

...DIAC OUTPUT IN HEART DISEASE AND FAILURE. The impor...ant is that the output of the heart cannot be raised to meet ...quirements of the body on exertion when there is disease of ...rt. When the inefficiency of the heart still further increases, ...tput may fail to supply the needs of the body at rest (2) ...tput is inadequate for the requirements of the body even in special circumstances when the actual level of the output is ...ely high

...TPUT IN ANÆMIA, EMPHYSEMA AND THYROTOXICOSIS. In ...ia the cardiac output is usually high This rise is due to an ...se in the stroke volume rather than to an increase in rate The high output seems to be independent of any elevation jugular venous pressure A raised output is needed in order to ...y the needs of the body for oxygen In severe anæmia the low ...n content of the blood may to some degree be balanced by a much raised output As the anæmia progressed the cardiac ... rose, and might be 6 5 or double the normal when the hæmo...n was below half (4) When the hæmoglobin falls below 20% ...output at rest may reach fourteen litres a minute (5) In ...ia the pulse pressure is high and there is overall vasodilatation ...count for this Despite the raised output it *is noteworthy that* ... is renal vasoconstriction, so the renal flow is low, and renal ...ia results (3) (see p 374)

emphysema the saturation of the arterial blood with oxygen ...ten as low as 70 per cent This may call for an increase in ...ut In some cases of heart failure from chronic pulmonary ...se the output was kept at normal level when at rest But ...xercise it could not be raised (7). In fact in some the cardiac

... course reduce the output. In these ...ents also the renal flow is poor, and the filtration fraction elevated ...) The degree of cyanosis and so of polycythæmia seem to be ...allel to the degree of failure

These rather conflicting factors may account for the varying ...els of cardiac output in chronic pulmonary disease It may be ...h, low, but is usually normal It is odd that the pressure may ...e in the pulmonary artery during failure, some 50% (to 37–57 ...m Hg) On recovery it falls It is possible that anoxia plays a ...rt in causing pulmonary arteriolar constriction; the increase in

pressure is more likely to be due to this than to increase in viscosity of the blood. These variable causes may thus vary the output *(8)*.

Thyrotoxicosis. Here the increase in the general metabolism demands more oxygen. The output of the heart is therefore increased, and with it the rate of the heart, and also the rate of the circulating blood (p 224).

Arteriovenous shunts. Here a relatively high output is needed to make good the loss of the shunted blood, so that the needs of the body, if possible, are supplied. In the case of the patent ductus arteriosus, and ventricular septal defects, and arteriovenous aneurysms these defects are obvious enough; as in other conditions, the left ventricular output tends to fall or be too low. Of particular interest is the increased vascularity of the bones in osteitis deformans (Paget's disease) *(2)* The shunt may vary in these cases. At rest the increase in flow through the bones may hardly matter, but on exercise an abnormal degree of increase in the cardiac output may be noticed. The vascularity of the affected bones varies a great deal, and with it the shunt. Probably about a third of the skeleton must be affected to raise the output In two cases the normal rise on exercise in output of 0·6–0 8 litres per minute per 100 ml. of oxygen consumed, reached as much as 12 and 22 litres per minute *(11)*. In beri-beri the heart failure tends to be of the high output type *(12)*. This is very rare.

Summary. There can be no doubt that the output of blood from the heart is a basic function which the needs of the body as a whole require to be maintained as long as possible When it falls, all tends to fail. When cardiac failure comes on the output may fall, at rest, to 80% of the patient's normal. It may drop to 60% and may be lower in cases where the signs of congestive failure are advanced And it is because the cardiac output is so low that the signs of heart failure are so grave In health the output increases with anxiety, hence the need for relaxation to get accurate readings. Exercise causes it to rise, but the weak heart cannot raise it enough for the occasion In thyrotoxicosis and severe anæmia the body needs for oxygen require a high output to be maintained; so that an output above the normal average may actually be insufficient, and the signs of congestive failure may be seen at the same time.

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Blood volume. Originally the volume of the blood was estimated by injecting 6 ml. of Evans Blue dye into a vein Samples of venous blood were taken from twenty to sixty minutes later, and the mean dilution of the dye estimated by a photo-electric colorimeter after removal of the plasma proteins The volume of the blood could then be calculated The normal figure varies with the size of the individual, the results in heart failure can be expressed as a percentage deviation from the predicted normal This method was probably accurate to within 10%

Labelled red cells have also been used Here 6 ml of blood are taken from the patient and mixed with radioactive phosphorus Three ml. are injected into the vein of one arm and specimens withdrawn from a cannula inserted into the brachial artery of the other arm The radioactivity of the specimens when equilibrium had been obtained, when compared with that of the original portion not injected, enables dilution to be calculated, and so the total amount of circulating red cells can be estimated When the volume of the packed red cells is known, the volume of the plasma can be obtained by the hæmatocrit, the sum of the two is the volume of the blood

In the same way red cells "tagged" with radioactive chromium (Cr^{51}) can also be used

Radioactive iodine (I^{131}) can be used to label human serum alb

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... some patients wasting may have altered their normal weight (*1*) There are some ... n these

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Venous pressure. *Starling's law* Starling showed that the force of the cardiac contraction depended on the length of the muscle fibres in diastole, this is determined by the pressure at which the heart is filled. When the chamber begins to fail this response to the increased tension of its fibres no longer occurs The output of the chamber will begin to fall

RIGHT VENTRICULAR PRESSURE. The cardiac catheter has provided the information Normally it varies in systole from 18 to 30 mm. Hg The diastolic pressure varies from -2 to $+2$ mm. Hg at the start, to 0 to $+4{\cdot}5$ mm Hg at the end of diastole. When the right ventricle fails the diastolic pressure increases up to twice the normal. The systolic pressure may rise if failure of the left side has raised the pressure in the pulmonary circuit

RIGHT AURICULAR PRESSURE The normal pressures vary from -2 to $+2$ mm Hg When the right ventricle fails the pressure in the auricle must rise, and may reach over 20 mm. Hg.

VENOUS WAVES During the cardiac cycle there are five auricular waves The first is positive (a) This is due to auricular systole The second is positive (c) due to closing of the tricuspid valve on systole of the ventricles The third is negative (x), and marks the fall in pressure due to the descent of the heart on ventricular systole Then comes the positive wave (v) due to rapid filling of the atrium, and lastly, the fifth wave (y) which is negative, and due to fall in auricular pressure on the flow of blood into ventricle when the tricuspid valve opens

THE VENOUS PRESSURE Careful [illegible]
ir [illegible]
o [illegible]
a [illegible] available for the measurement [illegible]

[illegible] venous pressure varies from 50 to 140 mm water Forced inspiration against a closed glottis lowers the pressure (Muller) forced expiration similarly raises it (Valsalva) The contractions of the muscles on exercise forces more blood into

whole the volume of the packed red cells is raised more than that of the plasma *(3)*. But the plasma volume is raised, too *(4)*. On recovery there is a return towards the normal; the plasma level falls first, and the red cells more slowly *(4)*. It is in failure of the right ventricle that the volume increases, not so much with insufficiency of the left ventricle, or with mitral stenosis *(5)*. When the heart is greatly enlarged the residual blood in it may account for some of the rise in volume *(6)*. Using P_{32} labelled cells, it appeared that two litres at least might well be ascribed to this residual blood There is a relationship with the amount of œdema *(2)*

It is not understood exactly how the increase in the volume of the blood comes about, nor the reason for it It seems likely to be first of all associated with retention of fluid. This will be followed by the formation of more proteins in the plasma, and then by an increased formation of red cells Possibly anoxæmia may stimulate the bone marrow When normal persons consumed a large quantity of salt their blood volumes rose and their weights increased. The same results, even to the reproduction of a state of congestive heart failure, has been brought about by giving much salt to patients who had recovered from congestive failure. Once œdema is present to any degree, possibly the increased pressure of the extra-cellular fluid as well perhaps as the increased protein in the plasma, allows a larger volume of blood to remain in the circulation. There is no very close correlation between the level of the venous pressure and the volume of the blood One may rise without the other. In severe anæmia, for instance, the blood volume may be low, but the pressure in the right auricle raised.

Summary. The volume of the blood is increased in congestive heart failure, anything up to 50% of the normal This accounts for some of the increase in weight of the patient *(4, 7)* At the same time the rise in the interstitial fluid volume is also more, anything up to 100% of normal. This fluid is transferred from the plasma The accumulation of fluid in the body is shown by a *positive* water balance. This results from a diminished rate of filtration through the glomeruli *and an increased reabsorption of water by the tubules* [illegible] excessive

[illegible]

be aided by the dilution of the plasma proteins by the retained water and a lowering of these osmotic pressures. Possibly the formation of new protein never quite keeps pace with the tendency to a rise in blood volume (2).

veins are very distended, reaching the angle of the jaw. If the vein is closed by the finger at the top of the neck the level of pulsation can often be seen below the obstruction Gross venous distension may affect the lingual veins, and higher still the retinal veins. Jugular pulsation can easily be distinguished from carotid pulsation, the sharp arterial thrust is wanting. The external jugular is often seen easily, but the internal is more reliable The rise of pressure on exercise is exaggerated if failure is coming on (5). Intravenous infusions, elevation of the legs, compression of the abdomen all cause the venous pressure to rise to a degree not seen in health (6). The possible causes of the raised pressure have attracted attention. Retention of sodium is not parallel to the rise in venous pressure (7). Minor rises in venous pressure do not affect the kidneys (8). The sodium retention comes before the rise in the venous pressure (9) It is possible that there may be a state of diminished venous distensibility, in fact a peripheral venoconstriction. There appears to be less blood than normal in a limb for a given venous pressure (10). There is no constant association between the volume of the blood and the pressure in the veins, the venous tone may be the important point (11) There is also the possibility of some redistribution of the blood to the venous side of the circulation, without any increase in its volume (12) Most conspicuous venous pulsation is seen in systole with tricuspid incompetence The cardiac forward output is falling, and the grossly raised venous pressure may be due to the reduced forward flow (13)

Venesection. Studies with the cardiac catheter have given varying results Sometimes withdrawal of blood caused the right auricular pressure to fall (14), without change in the cardiac output,

influx, venesection allows a lower filling pressure and so less distension of the right ventricle, which may lessen the regurgitation (14)

Left-sided failure. By means of the cardiac catheter it has been possible to study the hæmodynamics of veins in the lungs behind the left ventricle The capillary "wedge" pressures in the lungs gives those of the left auricle The results are quite in keeping with those obtained on the right side. The excessive filling of the pulmonary

the heart and raises the pressure. The Bainbridge reflex quickens the heart rate, the output increases and the venous pressure falls again

VENOUS PRESSURE IN CARDIAC FAILURE. When there is right ventricular failure the venous pressure may rise to 280 or 380 mm. H_2O if the failure is severe. The gradient of pressure from the vein in the arm to the auricle diminishes, and the flow in systole is reversed. *Auricular pulsations may be seen far along the veins. In* less severe failure the pressure in the veins may range from 150 to 250 mm. H_2O. When sitting the pressure readings are 80 mm. less than when supine. Pressure on the liver often leads to a rise in jugular pressure *early in failure (hepato-jugular reflux).* This is a useful early sign of congestion of the liver. The liver is always enlarged when there is a venous pressure of 220 mm. H_2O. If it is at a level of 250 mm H_2O there is usually ascites. The venous pressure may fall before the anasarca and hepatic enlargement have gone

TAMPONADE. Due to pericardial effusion or pericardial constriction, this causes a rise in the venous pressure The right ventricular pressure may be high at the end of diastole. Variations in the venous pressure in this condition do not affect the output, the constricted sac or the effusion prevent it

ATRIAL PULSES. In congestive heart failure the form of the right *atrial pressure curve is changed The "x" descent is less when there is a* moderate rise in venous pressure, with greater rises in pressure a positive systolic wave may be found *(1)* This suggests actual tricuspid regurgitation *(2)* If there is gross tricuspid incompetence *the forward flow occurs mainly in diastole*, the flow forwards from the superior vena cava, which occurs as the base of the heart descends on ventricular systole, is interfered with

Hæmodynamics. If there is heart failure and tricuspid reflux, the flow backwards may equal or exceed the cardiac output forwards *(3)*. The result is that despite a low output from the right ventricle forwards, the actual total output is large because of the large volume of blood pumped backwards Exercise will actually increase the reflux at the expense of the forward output This reflux may increase the work if the forward output of the right ventricle is low and fixed *(4)*.

Clinical observations. The method introduced by Lewis is adequate for ordinary purposes The patient should recline at an angle of 45° when recumbent, the normal pulsations studied by Mackenzie are seen The maximum pulsation can be studied when the jugular *vein is collapsing;* it cannot be seen easily if the

the liver loses its tenderness and becomes very hard. The development of cardiac cirrhosis of the liver is now under way. The liver function tests show a rise in the bilirubin in the blood, the alkaline phosphatase is increased later the flocculation tests give abnormal readings. If the patient lives long enough, there may be true portal obstruction and ascites as the result. It is possible that the defects in the liver may help to lower the proteins in the plasma. No doubt the cardiac cachexia that marks the end of chronic heart failure is to some degree hepatic in origin.

395.

1, 537.

J. 44, 571.

Rate of flow of the blood ... cross section of the vasc... ing in speed gradually ... slowest in the capillaries, in the veins the speed increases as the blood approaches the heart In former years much interest was shown in the measurement of the rate of the circulation. Little attention has been paid to the matter in recent years ...

Fluorescine. 5 ml are injected and the greenish appearance of the lips noted on its arrival under ultra-violet light. This is an objective test Normal time 15–17 sec

diseased; after a moderate rise the output falls. As a result of increased pressure, primary or secondary, in the pulmonary vessels, the pressure in the right ventricle rises. The diastolic pressure remains normal. When the ventricle ceases to empty properly because of enfeebled contraction, its diastolic pressure will begin to rise. This increase raises the auricular filling pressure (systolic pressure). Residual blood remains in the auricle as its diastolic pressure in turn increases, and so the filling pressure in the great veins goes up. Finally the gradient of pressure between them and the peripheral veins gets smaller Up to a point the rise in filling pressure may stimulate the stretched muscle fibres to still further effort to raise the output; but failure to do so is the inevitable result. Stretching of the walls of the right ventricle may still further aggravate the vicious circle by introducing the factor of the tricuspid reflux to increase the venous engorgement and reduce the output forwards How far increase in the volume of the blood, or hypothetical transference to the venous side plays a part in the early stages is dubious But in the later and grosser phases of circulatory breakdown they may make things worse

RESTRICTION OF VENOUS RETURN. As a temporary measure in an acute emergency of failure, letting the legs hang down reduces the return flow of blood. Mechanical obstruction by a bandage at the top of the thighs may help for a short time It has been suggested that the load on the right side of the heart may be lifted if the inferior vena cava be ligated below the renal veins. Some half of the cases were better for two years (*16*). In another series the shadow of the heart got less, but a quarter were dead in the first year. The operation is difficult, and there is danger of bleeding Patients should not be too young Cases of valvular disease did best (*17*)

THE LIVER. Engorgement of the liver may come on fast and cause pain *and tenderness in the right hypochondrium* It is a convenient reservoir for blood that cannot be cleared by the right side of the heart. The later stages, the nutmeg liver of chronic venous engorgement, with atrophy and accumulation of red cells at the centre of the lobule, and fatty degeneration at the periphery, is familiar to all. When there has been severe engorgement for a long time, as in tricuspid regurgitation, jaundice may be obvious. The bilirubin in the blood usually gives a mixed reaction, direct and indirect. The degree of jaundice is usually parallel to the degree of heart failure If the congestion clears up the jaundice disappears If it remains there is reason to suppose that there is permanent damage (*18*). After months of *engorgement, as in tricuspid disease,*

ventricular failure the slow passage through the pulmonary circulation may be very striking

Summary. The rate of the flow of the blood slows in heart failure This slowing mostly starts in the pulmonary circulation, and is enhanced when the systemic venous pressure rises Stagnation in the greatly enlarged heart causes further slowing, or may even interfere with the result From a practical point of view these tests may be of some help in assessing the gravity of cardiac symptoms, such as dyspnœa, which may be due to other things. They may be helpful in gauging the efficiency of the maintenance of the circulation after an infarct of the myocardium.

SECONDARY EFFECTS AND SIGNS OF CARDIAC FAILURE

The signs of heart failure can be divided into those mainly due to disturbances in the pulmonary circulation: dyspnœa, orthopnœa, cardiac asthma, pulmonary œdema, hæmoptysis and hydrothorax, and those due to derangements in the systemic circulation: peripheral œdema, venous and hepatic engorgement, and cyanosis. The first group is more directly related to primary left ventricular failure, except perhaps hydrothorax, and also to the effects of mitral disease—the second group follows failure of the right ventricle, which may be either primary or secondary to left-sided weakness

Dyspnœa [illegible] the earliest sy[illegible] failure The tendency to dyspnœa increases as the reserve power of the heart diminishes, for the heart becomes less and less able to meet the demands made upon it Finally, as failure gets worse, the patient is short of breath even at rest, and becomes orth[illegible]

INCREASE IN RESPIRATION Increase in breathing on exertion is a natural mechanism in healthy persons, whereby the body obtains the extra oxygen that increased muscular activity demands, and

Histamine causes a flush, not always easily seen, a salt taste and sometimes a sharp headache. Bronchospasm may come on. The test is both objective and subjective. An ampoule of 0·75 ml. containing 0·125 of histamine is suitable. Normal time 20–25 sec.

Sodium cyanide. Stimulates the vagal endings in the carotid sinus. The dose is 0·3–0·5 ml. of 2% solution. A sudden sharp inspiration is provoked: both subjective and objective Normal time is from 9 to 21 sec.

Sodium taurocholate (Decholin) causes a bitter taste: subjective only 5 ml. of 20% solution used—it is rather a large injection to put in quickly. Normal time 10–16 sec. Vomiting may be caused

Ether. This has been used to measure the arm to lung time The smell or taste of ether in the breath marks the end point. Normal time about 6 sec., local pain and thrombosis are not uncommon after the injection

Amyl nitrite This is suddenly inhaled, and the flush noted Normal time 14–25 sec There may be a headache It is not an accurate test

These tests all have some disadvantages, and the normal range is very wide: depending on the rate of the heart, nervousness and so on Those that are only subjective are very unreliable

Dye dilution curves. Probably the most satisfactory method is to measure the time of passage of an injected dye by an oximeter applied to the lobe of the ear. This needs special apparatus, of course, but is entirely objective. Tagged red cells can also be used

Abnormal circulatory rates. There are certain conditions where the rate is increased These are thyrotoxicosis, severe anæmia, and to some degree in emphysema. It will be noted that these are the states in which there is a tendency for the cardiac output to be increased and high output failure is found There is a tendency for the speed to rise in pregnancy. In myxœdema and polycythæmia vera the rate tends to be slow

HEART DISEASE WITHOUT SYMPTOMS. The rate is normal, it may be a little slow if the heart is large but if there is great enlargement there will probably be symptoms Minor variations in rate cannot be significant.

HEART FAILURE The fall in rate is very considerable The flow may be slowed to thrice the normal time Much of the slowing takes place in the lungs, and there is some relation to the diminished vital capacity. The presence of venous engorgement slows the flow into the heart. When the heart is greatly enlarged the injected substance may be lost or diluted in the residual blood In pure left

ventricular failure the slow passage through the pulmonary circulation may be very striking

Summary. The rate of the flow of the blood slows in heart failure This slowing mostly starts in the pulmonary circulation, and is enhanced when the systemic venous pressure rises Stagnation in the greatly enlarged heart causes further slowing, or may even interfere with the result From a practical point of view these tests may be of some help in assessing the gravity of cardiac symptoms, such as dyspnœa, which may be due to other things They may be helpful in gauging the efficiency of the maintenance of the circulation after an infarct of the myocardium

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Disturbances in the Pulmonary Circulation

Dyspnœa. Undue shortness of breath on exertion is often the earliest symptom of cardiac failure The tendency to dyspnœa increases as the reserve power of the heart diminishes, for the heart becomes less and less able to meet the demands made upon it Finally, as failure gets worse, the patient is short of breath even at rest and becomes orth—

INCREASE IN RESPIRATION Increase in breathing on exertion is a natural mechanism in healthy persons, whereby the body obtains the extra oxygen that increased muscular activity demands, and

eliminates the extra carbon dioxide that results therefrom Muscular activity alone can accelerate the rate of breathing by a nervous reflex. An increase in the pressure in the great veins or in the right auricle will stimulate the respiratory centre; perfusion of the lungs and distension of the pulmonary capillaries will stimulate respiration. The efferent path in all these reflexes is the vagus nerve, for they are abolished when it is cut These reflexes are linked with the rise in venous pressure which muscular contraction causes, by driving more blood back to the heart In health the circulation is adjusted to the needs of the body by raising the output of the heart, which may reach twenty or more litres a minute The diseased heart is unable to accomplish this increase in the output; the rise in the venous pressure is greater and more prolonged than in normal persons. This rise in the systemic venous pressure must reflect the rise in the pressure of the pulmonary veins and pulmonary circulation generally. There is increased "stiffness" in pulmonary tissues due to the raised pulmonary venous pressure. The chemical causes of an increase in breathing do not come into action until late in heart failure

Diminished vital capacity. The vital capacity is the figure of the largest volume of air that can be expelled from the lungs after the deepest possible breath In order to get a significant result the volume should be standardised against the amount which is normal for a person of similar body-area. The vital capacity varies a good deal with physical fitness, and improves with practice The normal average in males is 4,000 c ml. It is decreased in obesity, pulmonary disease, thyrotoxicosis and neuro-circulatory asthenia In heart failure the level may fall to a litre. In congestive heart failure the patient is unable to take a deep breath, but at the same time he is urged to increase his breathing The sensation of dyspnœa varies directly as the degree of ventilation required, and inversely as the vital capacity, or the ability to ventilate.

Pulmonary congestion. The pressure rises in the pulmonary artery and right ventricle in left ventricular failure It may be twice the normal, but not so high as in mitral stenosis where there is obstruction. The circulation rate in the lungs is much slowed, the times reaching two or three times the normal Some of the slowing is due to the residual blood in the heart, but much occurs in the pulmonary circulation and indicates stagnation in the vessels The engorgement of the pulmonary veins can be seen in the enlargement of the shadows of the lung roots in skiagrams of patients with left ventricular failure (Fig. 124) Engorgement of the pulmonary circulation stimulates respiration. congested vessels impair the

elasticity of the lungs, so that there is a lack of distensibility. At the end of expiration the pressure in the pleural sac may actually be positive, as a result of this inspiration will need a greater effort to increase it. The end of the story is to be seen in the "brown induration" found at autopsy. The lungs are stiff, hard and inelastic, and sections show tinged capillaries in thickened alveolar walls

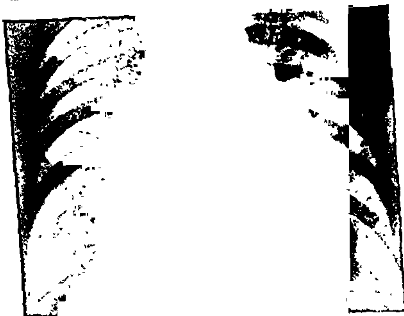


FIG. 124 Congestion of pulmonary veins in heart failure

Summary. Cardiac dyspnœa is due to the combination of two factors a call for increased ventilation and the inability to breathe deeply in response The *first* is due to reflexes arising as a result of the increase in venous and *pulmonary* pressure on exertion, the second to the increase of blood in the lungs, and later to the histological changes in structure this persistent engorgement causes As heart failure progresses the venous and pulmonary pressures become permanently raised, and the patient becomes orthopnœic

Orthopnœa. The patient is short of breath even at rest, and cannot lie flat in bed The number of pillows required is a practical guide to the severity of the affliction Finally, the patient may have to lean forward supporting his head on a bed-rest, or spend

his night in a chair. There is left ventricular filling failure, for the pressure in it at the end of diastole rises, and the pulmonary venous pressure follows suit even above the osmotic pressure Sitting up affords some ease by lowering the venous pressure on the average some 8 cm. of water—this lessens the stimulation of the respiratory centre There is also a fall in the output of the heart by a litre or so a minute, so the work of the heart is lowered The vital capacity is increased, for in the upright position the accessory muscles of respiration can best be used. The spine can be straightened to increase the capacity of the chest. The upward pressure on the diaphragm by the enlarged liver and possibly ascites, is reduced, and inspiration made easier.

ACUTE PAROXYSMAL CARDIAC DYSPNŒA If the cardiac efficiency has deteriorated rapidly, in these more severe grades of disability, there may be acute paroxysms of dyspnœa. These attacks may be brought on by over-exertion; or emotional stress, or by sudden weakness of the myocardium caused by an infarct. They are a feature of hypertensive heart failure and aortic valvular disease. They are sometimes seen in mitral stenosis, particularly in pregnancy. The underlying cause is the development of severe engorgement of the pulmonary circulation. This engorgement arises most commonly in the recumbent posture All these types have much reduced vital capacity There is a lowered velocity of the airflow, due to an obstructive difficulty especially in hypertension, in emphysema the conditions are rather similar. The cases of mitral disease are not prone to this bronchospasm (*1*)

NOCTURNAL DYSPNŒA Patients with much pulmonary congestion due to failure of the left ventricle under the burden of hypertension, or aortic valvular disease, or with severe ischæmic lesions, or wit

nal dy

After

feeling of imminent suffocation which makes him spring up panting for breath. He may sit up in bed or get out and go to a window for more air. If he is seen during the height of an attack he will appear pale, anxious, restless, sweating profusely with cold perspiration, breathing rather fast, but with shallow laboured breaths Inspiration is grunting and short, expiration is usually prolonged Sometimes there is a definite wheeze Cyanosis will be present if the attack is severe The pulse is rapid, the blood pressure, systolic and diastolic is usually raised, sometimes to a surprising degree although the pulse pressure may be low The pulmonary second

sound is loud At the bases of the lungs there may be a few moist râles, the upper lobe may be hyperresonant. Breath sounds are noisy and sometimes prolonged and wheezing. The attack may be over in a few minutes or last up to an hour At the end of the attack a little mucus, sometimes bloodstained, may be coughed up. Œdema tends to be more severe towards the end of a prolonged attack Râles are more profuse, there is a short dry persistent cough, dyspnœa becomes still more intense.

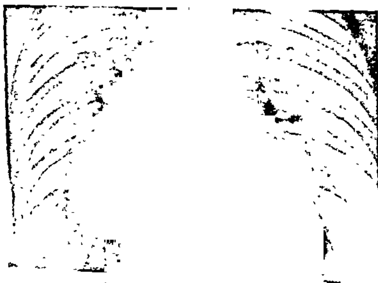


FIG 125 Acute pulmonary œdema

to
in
increases, the crepitations in the lungs
become coarser and more profuse. The blood pressure remains high, but the pulse is rapid and feeble The cough may now produce profuse pinkish watery frothy expectoration If the patient is being examined with the screen as the attack comes on, the dark cloud spreading from the roots of the lungs has a menacing aspect (Fig 125). A state of shock develops and the blood pressure now falls The condition is one of great danger, and the patient may die

Causation In cases where there has been too rapid transfusion of

fluid into the circulation acute pulmonary œdema has occurred All the typical features appeared. The vital capacity fell, the lung fields became less translucent and the shadow of the vessels far denser. There was increase in the size of the heart and the patients felt constriction in the chest *(2)*. As in other forms of œdema in the body, the question of the balance of osmotic and hydrostatic pressures in the pulmonary capillary bed is the important one *(3)*. Cases with mitral stenosis have been studied by the cardiac catheter. The pressure with the catheter wedged at the periphery (which is actually the capillary pressure) is normally 5–10 mm. Hg, but this may rise to over 50 mm. Hg, and as a result pulmonary œdema comes on. This is far above the osmotic pressure of the plasma proteins, which of course retains the fluid In the spongy lung tissue the stage is set for a profuse transudation into the alveoli The curious thing is that it does not happen more often in mitral stenosis, and is so frequent in failure of the left ventricle The reason appears to be the thickening of the capillary walls, which may be twice the normal, reaching 15 μ. The chronic high pressure in mitral stenosis causes this protective thickening; which is not there to prevent the transudation resulting from a sudden acute rise in pressure such as happens in hypertension It is possible that anoxæmia may increase permeability. and finally there is some obscure neurogenic cause which appears to have an influence, as those cases of acute œdema following brain injury would indicate.

CAUSATION OF ACUTE PAROXYSMAL CARDIAC DYSPNŒA It is fairly easy to understand how an acute sudden failure of a weak left ventricle may set up a desperate state of dyspnœa if the patient unwisely does too much But the classical attacks come on at night during sleep The dominant cause seems to be postural, the patient slips down in bed during sleep Lying down, the venous filling pressure is higher and the heart's output greater Breathing is less easy Difficulties then arise during sleep which reach a degree of acute embarrassment, and the patient awakes with a start and the attack begins The exciting causes, which have been called "triggers" may be coughing, dreams, visceral distension, or too much activity on the day before may have weakened the heart Breathing becomes wheezing, and expiration is as difficult as inspiration. This obstructive difficulty lowers the velocity of the air-flow. The loss of pulmonary elasticity, if there is emphysema, aggravates these troubles *(1)*. Records of breathing in patients with cardiac dyspnœa at rest, and with bronchial asthma, showed that the expiratory phase was much longer than in normal subjects. These

were able to shorten expiration, and so increase the rate of breathing; but in the cardiac and asthmatic patients the inspiratory and expiratory ratio remained the same. An intravenous injection of aminophylin (0 24 gramme) quickly shortened expiration (4). During an attack the venous pressure becomes very high; the pulmonary congestion increases, and sets up a reflex bronchospasm through the vagus (5)

Summary. Acute cardiac dyspnœa, sometimes called "cardiac asthma" is due to failure of the left ventricle causing intense engorgement of the lung Obstruction at the mitral valve may also cause this overfilling of the pulmonary circulation When the pressure in the capillaries becomes very high acute pulmonary œdema comes on In some cases a reflex spasm of the bronchioles plays an important part

Treatment. Early in an attack the progress may be stopped by pressing on the carotid sinus, thus setting up a depressor reflex Morphine, preferably given intravenously (⅙–¼ grain, 15–10 *mg.*) is quick and effective in action It may be combined with aminophylin (0 4 gramme) particularly if there is bronchospasm It is useful to add digoxin (0 25–0 50 mg) This will stimulate systole, and along with aminophylin may reduce venous pressure to some degree It is of course essential if there is auricular fibrillation If the venous pressure is very high, and response to the drugs given by injection is not [illegible]

[illegible] during sleep is not easy Very little should be eaten in the evening, and the bladder should be emptied the last thing at night

Adrenalin should not be given for the bronchospasm of acute left ventricular failure Most of these patients are hypertensive, and the pressure during an attack is usually higher than ever.

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3 Hayward, G W 1955 *Brit med J* 1, 1361.
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Derangements in the Systemic Circulation

Cyanosis *is due to the actual amount of reduced hæmoglobin in the blood* In the veins there are usually 6 volumes per 100 ml. If there is 6·7% in the capillaries the patient looks blue at that spot. If there is anæmia as grave as 30% of hæmoglobin, cyanosis is impossible. If the hæmoglobin is 120% of normal, the blueness is all the more intense

Peripheral cyanosis is seen in the lips, ears, fingers and toes and cheeks. It is usually due to cold slowing down the circulation by constricting the arterioles, while the capillaries are dilated. The slow passage of blood leads to an abnormal loss of oxygen In all these areas the subpapillary venous plexuses are highly developed In the face venules are often conspicuous. A raised venous pressure may lead to stagnation and cyanosis at the periphery, as well as a low output from the left ventricle

Central cyanosis. Here the cyanosis is seen in the warm parts, notably in the tongue and inside the mouth, and in the retinæ

Central cyanosis may be cardiac or pulmonary. A shunt in the heart allowing a flow from right to left is the usual cardiac cause These are the congenital defects such as the Tetralogy of Fallot, reversal of left to right shunts, transposition of the great vessels and so on.

Pulmonary causes operate when the state of the lungs interferes with the oxygenation of the blood, as in emphysema, when the arterial saturation with oxygen falls to 70% and lower Œdema will tend to hide cyanosis Very swollen legs are white, but the face and hands may be blue

Mitral stenosis has both peripheral and central cyanosis which may cause such a characteristic facies. Cyanosis seems to develop from peripheral stagnation due to low output, to which may be later added a central cause, venous back pressure, and also centrally diminished permeability of the pulmonary capillaries, and perhaps local dilatation of venules and capillaries The degree of cyanosis is usually parallel to the degree of polycythæmia and increase in hæmoglobin—clubbing of the fingers is in keeping it is most conspicuous in the young with congenital cardiac cyanotic defects, it is less obvious in the elderly with mitral stenosis or emphysema.

OXYGEN. In most cases of heart failure there is no fall in the saturation of the arterial blood with oxygen Cyanosis occurs, apart from intracardiac or pulmonary shunts as a result of pulmonary disease.

Administration of oxygen. An oxygen tent is the most effective, the patient then breathes 40–50% pure oxygen. Some patients object to the heat and stuffiness A B L B mask or bag is useful and can be used intermittently A flow of six litres a minute will raise the alveolar oxygen to 80%, from the normal of 14%. Persistent coughing makes it difficult to use these devices.

The nasal catheter, with a flow of three litres a minute can raise the alveolar O_2 to 27% This method is well tolerated as a rule, and quite efficient for usual needs

It is an important point to remember that the respiratory centre seems to become used to a high level of CO_2 in the blood; so those who have suffered from cyanosis for a long time, such as those with advanced emphysema, may lack a stimulus to breathe if the alveolar O_2 is raised too high For such as these a tent may be dangerous, as apnœa may supervene For these the nasal catheter is adequate and safe Patients who are blue from a right to left shunt, as in congenital lesions of the heart or lungs, derive but little benefit from oxygen In peripheral cyanosis there is no improvement

Cardiac œdema. Heart failure sooner or later causes œdema Its first appearance in the dependent parts is of course due to gravity Various causes, some still not yet clear, appear to be at work

HYDROSTATIC CAUSES At the arterial end of the capillary loop the pressure of the blood is 32 *mm* Hg, at the venous end it is 12 *mm* Hg, when the subject is in the supine position. In the erect position the pressure in the capillaries of the feet is still higher The osmotic pressure of the proteins in the plasma, which is usually about 22 mm Hg, balances the hydrostatic pressure which tends to drive fluid out, and so it is retained But it is well known that swelling of the ankles is not of cardiac origin in most of the patients who complain of it, due to varicose veins, or poor muscles

Raised venous pressure Normally, in the arm veins the pressure is about 7 mm Hg lower than in the venous ends of the capillary loops Œdema is usually present when the pressure at the venous end of the capillary loop exceeds 20 *mm* Hg The average normal colloid osmotic pressure being 22 mm Hg, the critical point for venous pressure in the arms is 13 mm Hg In all stages of heart failure, if the pulmonary veins are included, the venous pressure is raised, and this will help to cause œdema But th[illegible]

[illegible] asions

[illegible] an be

[illegible] might

be expected to raise the pressure in the venous and capillary systems. It is doubtful whether this in itself is really important in many cases. The possibility of some reduction in the osmotic pressure of the plasma proteins has been noted. How far this feature of increased blood volume contributes to a rise in venous pressure is uncertain. There might have to be some increase in the tone of the veins, and there is some evidence that this may occur.

DIMINUTION OF THE PLASMA PROTEINS. In patients with long standing congestive heart failure the plasma proteins may be low This may be the result of deficient intake in the diet, or perhaps to liver deficiency due to prolonged congestion. Albuminuria causes loss of protein. This form of hypoproteinæmia is not very common, but sometimes the albumen in the plasma may be 25% of its normal level, and so the osmotic pressure of the colloids will be low enough to allow fluid to escape into the extra-cellular spaces

Renal causes. It is in the kidneys that the early and important causes of œdema must be sought Here occurs the retention of water that leads to the increase in the weight of the body The work of Warren and Stead first in 1944 and later of Merrill showed the importance of diminished flow of blood through the kidneys, and of the retention of sodium. Much work has been done in recent years to investigate further these disturbances in the metabolism of water and electrolytes.

RENAL FLOW. In patients with disease of the heart causing heart failure there is a definite fall in the effective flow of plasma through the kidneys. This is before failure has come on When there is congestive failure the flow may only be 25–30% of normal The rate of glomerular filtration is less affected and may be reduced only to 65 or 75% of normal This suggests that the glomerular pressure is raised by spasm of the efferent arteriole (*1*) Studies of pressure in the right auricle have shown that any rise here is not always a cause (*2*). This diminished renal flow is a cause of oliguria But this varies. There may be nocturia (*3*), so that the night volume is raised and the day volume lowered At night the filtration rate may rise 30% and the output of salt increase (*2*) This alteration may at first make good the day's deficiency, but later it is not seen, as then œdema appears (*2*). As congestive failure develops the renal flow falls still more. Its low level appears to be parallel to the severity of the disease, and is proportional to the fall in stroke volume (*7*). In the right ventricular failure following chronic pulmonary disease, the renal plasma flow falls and so does the glomerular filtration rate. Here possibly the lowered arterial oxygen

saturation may play an early part; in these causes, too, severe rise in venous pressure may be important (5). In other types the rise in venous pressure may come late or be less high (7)

RETENTION OF WATER. The retention of water may be a primary abnormality and lead to dilution of electrolytes, with slight hyponatræmia and hypochloræmia the retention of water being due to the antidiuretic hormone of the posterior part of the pituitary gland (8) But a rise in osmotic pressure will lead to increase in the secretion of antidiuretic hormone in order to retain water and dilute the electrolytes (5). It seems likely that this disturbance of the water volume is hormonal in nature, and not necessarily from retention of sodium (4).

RETENTION OF SODIUM The flow from the glomeruli falls, and so less sodium is presented to the tubules. They may reabsorb it completely (10) but there is in fact selective retention. It has been suggested that the salt-retaining corticoid aldosterone plays a part This acts in response to a decrease in extra-cellular osmolarity following retention of water, sodium chloride being retained to avoid dilution (11) It has been shown that there is such a substance.

... is (1) the constriction of the efferent renal arteriole, (2) the part played by the *antidiuretic* hormone, (3) the role of *some salt*-retaining substance, the first diminishing the flow of urine, the second causing retention of water, and the third *retention* of salt, which of these last *two acts first* is not certain, but together they can provide a vicious circle leading to gross œdema

Intracellular derangements. It is becoming evident that in addition to the *increase* of the extracellular fluids and their electrolytes, *important* changes take place within the cells of the ...

... potassium and sod...

cells to fall (*11, 14, 16*) This

(*12*) Potassium, sodium anc

(*11*) In fact it seems that ... fall in weight on treatment is too great to be due to loss of *extra*-cellular fluid alone and some must come from inside the cells (*16*) In heart failure ...

stress ...

in

pot

The presence of œdema interferes with the nutrition of all the tissues affected. The flow of blood is greater in an œdematous limb. The oxygen content in the blood of the femoral vein may be higher than usual, for the œdema acts as a barrier to the diffusion of oxygen, and so the tension of the oxygen in the tissues is diminished. It is clear that gross œdema is bad for the individual, and all efforts must be made to get rid of it.

Effusions. Hydrothorax is common in heart failure, but small *quantities can only be detected by radiology. When the rhythm is* normal the incidence of hydrothorax on the two sides is about normal. When there is fibrillation it is four times commoner on the right side. The association of this arrhythmia and the right-sided enlargement of mitral stenosis provides the link, through pressure on the root of the right lung Interlobar effusions on the right side are not uncommon. Usually the effusions are small and rarely need to be aspirated, particularly now that the mercurial diuretics are so efficient. But when one side of the chest is half full of fluid, aspiration will be needed Removal of the fluid lowers venous pressure and increases vital capacity. But this may not be apparent at once, as after aspiration the diaphragm rises if the collapsed lung does not expand at once.

Promotion of Diuresis and Relief of Œdema

DIURETIC DRUGS. The presence of œdema and oliguria is a call for diuretics *(17)*. The rate of urinary flow depends on:

1. The filtered load of water and solution.
2. The reabsorption of water in the distal tubule under control of the antidiuretic hormone.
3. The reabsorption of sodium and its ions, influenced by aldosterone *(17)*.

It is essential to relieve the body of water and solutes One may induce osmotic diuresis by · (1) increasing the amount of sodium filtered through the glomeruli, (2) decreasing the sodium reabsorbed by the tubules *(17)*

MERCURIAL DIURETICS These drugs have now long proved their value, and are the most valuable aids in the treatment of heart failure since Withering introduced digitalis in 1785 They act by inhibiting the reabsorption of chloride, and so of sodium, from the tubules. This is done by inhibiting succinic anhydrogenase activity in the cells of the loop of Henle

Mersalyl includes a salicylate group, and contains about 40% of mercury calculated on the dried weight. It is available in 10%

solution in 2 c ml. ampoules. *Neptal* includes a phenol ring and contains 9 20% of active substance weight/volume In both these is a small amount of theophylin, too little to be of use.

These drugs are given by intramuscular injection. The usual site in the gluteal area should be avoided if there is much local œdema, or the injection may not be absorbed, and very troublesome local sloughing may occur

Thiomerin can be given by subcutaneous injection, and is safe and effective (*19*) Oral tablets are useful, and are not toxic (*20*). The *intravenous administration* of these drugs can be dangerous, causing collapse, coma and sudden death.

Renal considerations The presence of albumen in a concentrated urine of high colour and specific gravity is no contra-indication. But if nephosclerosis is suspected in elderly patients, there may be increase of albuminuria, or hæmaturia may be caused This vetoes further administration.

It has been noted that the nephrotic syndrome may follow prolonged administration of mercurial diuretics The result may be fatal There is necrosis and fatty degeneration of the *convoluted tubules* The renal tissues may contain much mercury. Persistent and increasing proteinuria is the warning sign, after successful diuresis In these cases the usual fall in plasma proteins and rise in serum cholesterol is noted, the blood urea being normal or moderately raised (*54*, *55*)

If the urea in the blood is above 60 mg *per* 100 *ml* the *mercurial* diuretics are best not used.

Other reactions Stomatitis and hæmorrhagic colitis are rare nowadays Rashes are not often seen Neptal given by mouth may cause diarrhœa

Administration and action The injection is best given in the morning The diuresis may begin quite soon, in half an hour A satisfactory result may be 5 *or* 6 pints Hundreds of injections have been given over *many* years without harm, and have been indeed the means of keeping the patient alive The injections may be given as needed

The drug should be

ation rate is very low

2 l

in

...g). This is sometimes overlooked when the limbs are free from dropsy.

EFFECTS ON THE ELECTROLYTES These are not very common in this country, perhaps because the restriction of the intake of sodium may not be very strict. The disturbance in the electrolytes can be very unpleasant in their clinical consequences. The chief trouble concerns the loss of sodium (hyponatræmia) and the loss of chloride (hypochloræmia). This loss of chloride exceeds that of the sodium *(23)*. The loss of the acid ion leads to alkalosis *(22)*. There may also be deficiency of potassium and calcium. The continued use of powerful mercurial diuretics, combined with a really low intake of sodium, may cause the "low-sodium syndrome." This may be precipitated by withdrawal of large effusions, introducing the state of "depletion hyponatræmia" *(24)*.

The clinical picture is marked by an intractable state of œdema, which fails to respond to the mercurial diuretics. The symptoms are drowsiness, profound lethargy, fatigue and remarkable asthenia There are also anorexia, nausea and vomiting—which may aggravate the loss of chloride; there may be tiresome cramps *(25)*. The output of urine falls, the weight increases, owing to retention of fluid, this may be due to excessive intake of water. The urea in the blood rises, and investigations of the other electrolytes shows hyponatræmia and hypochloræmia *(25, 26, 27, 28)*. The removal of the chlorides precludes further removal of sodium by the mercury, the excessive loss of chloride causes alkalosis *(30)*. Two aspects may be considered: (1) absolute depletion of sodium, and (2) absolute excess of water. There may, in fact, be water intoxication, with pulmonary œdema, restlessness and convulsions *(28)*

The excessive hydration affects the body cells, and potassium is lost from them *(27)*, and this loss may be considerable *(31)* Actually diuresis leads to increase of potassium in the cells, and decrease of their water content

[illegible]

given intravenously *(29)* Corticosteroids and ACTH have been suggested, it is supposed that the former suppress the antidiuretic hormone *(34)*. They also favour retention of salt which may help to make good the low level in the blood of sodium and chlorine For hypokalæmia potassium citrate should be given. Potassium chloride would be needed in alkalosis.

OTHER DIURETICS Apart from the mercurial diuretics there are several new drugs that have a somewhat similar, though less potent action.

Acetazolamide (*Diamox*) This diuretic inhibits the enzyme, carbonic anhydrase The action of this enzyme is to cause the absorption of the sodium in the glomerular filtrate in exchange for the hydrogen ions liberated in the tubule cells. The failure to take up sodium leads to the escape of sodium bicarbonate and so water goes with it. The usual dose is 0 25–1 0 gramme in 24 hours After 3 or 4 days the excretion of sodium bicarbonate falls. There is a tendency to acidosis as a result of the loss of alkali and this may be actually useful in correcting hypochloræmic alkalosis due to mercurials, as the drug tends to cause hyperchloræmic acidosis Ammonium chloride can be given, too. The mercurials are three times as strong as acetazolamide (38) Acetazolamide is best given for 3 or 4 days at a time, and then left off for 2 or 3 days. Drowsiness and headache may occur. Loss of potassium has been reported (37) There may be response to a mercurial that has failed if it is given after a few days of diamox (26).

Aminometradine (*Mictine*) This is about half the strength of mersalyl About half the patients have nausea. Vomiting and diarrhœa

was rare

aminometradine. 2·4 grammes given over 48 hours were about equivalent in action to 2 ml. of mersalyl The usual dose is 400 mg (one pale green tablet) thrice daily for 2 days Tinnitus and deafness have been noted as a result of taking it The precise action on the kidney is not known The increase in the excretion of sodium and

xcre-
weak

and this may lead to hypokalæmia (51, 53) This loss may be made good by 3 or 4 grammes of

but it may well be combined with them, or used as a substitute in chronic cases where mercury cannot

be used, or if the dropsy is not really severe (*41, 42, 52*). Unpleasant effects are not encountered. It tends to lower the blood pressure

Xanthine derivatives. Theophylline (dimethylxanthine) is an isomer of theobromine. Theophylline-ethylene-diamine is the most potent. It is also called aminophyllin. As a diuretic these drugs increase the flow of blood through the kidneys. They can be given by mouth for diuretic purposes, but they are much less potent than the mercurial diuretics, or the other new drugs acting on the sodium and chloride metabolism Nowadays their part as diuretics is small But the value of theophylline-ethylene-diamine by intravenous injection for acute failure of the left ventricle is very great.

Urea. This may be effective 20–30 grammes daily are needed. It is unpleasant to take The urea in the blood will rise. It is supposed that it leads to the retention of water in the tubules for its elimination (*43*), for it is filtered through the glomeruli

Digitalis must be mentioned. After all, its first reputation was gained as a cure for the dropsy (Withering) Nowadays the prompt use of the mercurial diuretics makes its action less conspicuous But one would not rely on it alone, its success is perhaps confined to patients with the fast rate of auricular fibrillation In one series it worked in one-third of cases only (*44*)

Sodium restriction. The realisation that retention of sodium was really the important cause of cardiac œdema led to the planning of a diet to avoid its intake, and to measures to prevent its absorption

DIET. The severity of restriction of sodium must depend on the severity of the heart failure This can be graded by their tolerance of sodium. If heart failure is mild the patient might be able to take 4–10 grammes of salt daily (*24*) An ordinary diet without added salt provides about 4 grammes of salt daily With moderate heart failure 2–3 grammes of sodium chloride might be tolerated If no salt is used in cooking the intake of sodium chloride is reduced to 2½ grammes If the heart failure is severe, œdema can only be kept under control by limiting the salt intake to 0·5–1 0 grammes which amounts to 200–400 mg of sodium. While the low sodium diet is of extreme importance in cases of *intractable* heart failure it is unnecessary to prescribe the most rigid diet for all cases But the use of salt-free bread and salt-free butter is the most important difference between the moderate diet and the severe But sheets for 200 mg. Na (0 5 gramme salt) and for 500 mg Na (1 25 gramme salt) are given on pages 381–382 as examples

200 mg. SODIUM DIET

Breakfast	1 oz. bread—salt free Salt-free butter as desired. ¼ oz. marmalade or jam Serving fresh or stewed fruit with sugar. Cup of tea with 1 oz milk.
Mid morning	Fruit drink with glucose, *or* sugar as permitted
Dinner	2 oz meat *or* 1½ oz fish 2 oz potato—salt free. Green vegetables 2 oz —salt free Cereal pudding with 5 oz. milk, ½ oz. sago, semolina, etc., *not* cornflour
Tea	1 oz. bread—salt free. Butter—salt free ½ oz. jam 2 oz milk in tea
Supper	1 oz meat or low salt dish 2 oz potato 1 oz salt-free bread Salt free butter Helping fresh *or* stewed fruit

The patient may eat fresh fruit and boiled sweets but no other extras

	Oz	Na	C	P	F
Bread—salt free	3	12 8	45	9	1 5
Meat	3	60		21	15
Potato	4	4	12	1 2	
Green vegetables	2	7 6			
Milk	8	113 6	12	8	10
Sago, semolina, etc	½	1	10	1	
Jam	½	2	8		
Marmalade	¼	1 3	4		
Fruit	12		30		
Sugar—glucose	3	Tr	90		
Butter—salt free	1				25
	37¼	202 3	211	43 2	51 5

Total calories 1500

CHO	300 gm
Protein	70 gm
Fat	85 gm
Calories	2250

500 mg. SODIUM DIET

Daily	1 pint milk—to be used for all drinks, puddings, etc
Breakfast	Shredded wheat, puffed wheat, porridge cooked without salt, or fruit if desired. 1 egg—boiled, poached, scrambled or fried.
or	A helping of white fish,
or	Fried salt-free bread and tomatoes. 2 slices salt-free bread with unsalted butter. Marmalade or jam. Sugar as desired. Tea or coffee with milk from allowance.
Mid-morning	Tea, coffee or fruit juice
Dinner	Average helping of meat, fish, rabbit, liver or poultry, cooked without salt Potato and vegetable cooked without salt. Pudding or sweet.
Tea	2 slices salt-free bread with unsalted butter Jam. Tomato or salad if desired Tea, sugar, milk from allowance. Biscuit, cake or tart.
Supper	As for dinner.

NO SALT TO BE USED IN COOKING OR AT TABLE

The strict rice diet is effective but disliked by patients for any length of time.

The intake of fluids may be guided by the advice of Withering, who allowed the patients to drink "whatever they prefer, and in as great quantity as their appetite for drink demands." This applies, of course, to water. Beer contains much sodium, and so do such beverages as Bovril. Fruit juices may contain a good deal of potassium Drugs containing sodium are often overlooked, and must be avoided There are various substitutes for salt, but none provides the real flavour Lemon juice often makes some things more palatable

Resins. These may be useful in preventing the absorption of sodium from the gut. In some way they may promote the action of the mercurial diuretics on the kidneys (*45*). In some cases they may take the place of these drugs and so help to avoid the low-sodium syndrome (*46*).

[illegible] the patient's response

[illegible]

level and alkali reserve in the [illegible]

Hyperchloræmia may come on and hypopotassæmia sometimes. These preparations are unpleasant to take, and upset the digestion

Their clinical value seems to be rather limited But in some cases of obstinate œdema they are worth bearing in mind. But there are

sodium chloride content may be low, and sometimes there is a considerable cloud of albumen. Urates are plentiful, and the reaction acid The albumen is parallel to the degree of failure (50). It is no contra-indication to mercurials. But if the urine is pale and the specific gravity lower than 1015, with less albumen, nephrosclerosis may be present, especially in elderly hypertensive patients A rise in the blood urea may be suspected This may parallel the

circumstances there may be large accumulations in the abdomen, as in constrictive pericarditis, or cardiac cirrhosis of the liver, or in the chest The legs may be drained by multiple punctures or Southey's tubes under cover of penicillin In order to obtain the maximum effect the patient should be sitting-up with the legs dependent for twelve hours Drainage of the legs may remove ascites It may be necessary to tap the abdomen or the chest if the effusion embarrasses the breathing seriously Once the ascites is removed the kidneys may respond better to diuretics It must be remembered that a good deal of sodium chloride and protein may be removed from the body by these procedures

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Effects of Changes in Electrolytes on the Cardiogram

Abnormalities in the cardiogram are not likely to be seen in the relatively mild states arising from diuretics, particularly as they mainly concern variations in the level of sodium But potassium may fall with the exhibition of saluric This seems to be the place to mention the cardiographic abnormalities met with in certain abnormal levels of some electrolytes.

POTASSIUM. It should be remembered that on depolarisation of the muscle cell the potassium ions move out, and the sodium ions move in On repolarisation potassium moves in, and sodium out.

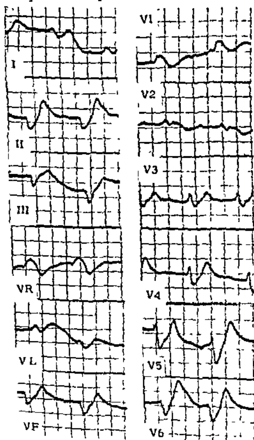


FIG 126 Hyperkalæmia.
Serum K^+ = 7 8 m Eq /l (30 4 mg /100 ml) Normal 3 5 to 5 5 m Eq. l

The level of potassium in the cell is higher than that ... level of ...

h

... sign is the high-peaked T wave. This appears when the K reaches 7 m eq per litre (normal level about

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Effects of

Abnormalitie n the relatively mild they mainly concern variations in the level of sodium But potassium may fall with the exhibition of saluric This seems to be the place to mention the cardiographic abnormalities met with in certain abnormal levels of some electrolytes

POTASSIUM. It should be remembered that on depolarisation of the muscle cell the potassium ions move out, and the sodium ions move in On repolarisation potassium moves in, and sodium out

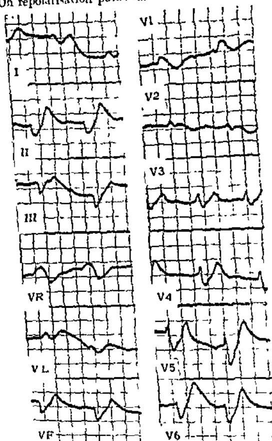


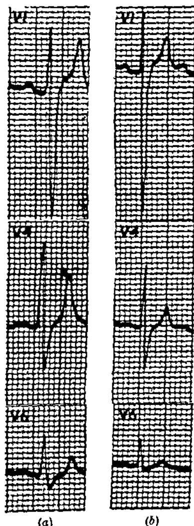
FIG 126 Hyperkalæmia
Serum K+ = 7 8 m Eq /l (30 4 mg /100 ml) Normal 3 5 to 5 5 m Eq l

The level of potassium in the cell is higher than that outside. The level of sodium is lower inside.

Increase of *extra*-cellular potassium will slow depolarisation and hasten repolarisation. Increase of extra-cellular sodium will hasten depolarisation and slow repolarisation (*1*)

Hyperkalæmia The first sign is the high-peaked T wave This appears when the K reaches 7 m eq per litre (normal level about

5 m. eq. per litre Later QRS is prolonged, and may resemble bundle branch block; A-V conduction is prolonged; later P waves disappear as auricular standstill comes on. Finally ventricular fibrillation may come on if the extra-cellular K concentration reaches



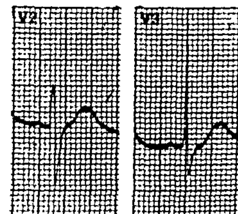


FIG 128. Hypokalæmia.
Serum K+ 9 mg./100 ml
Normal 14-22 mg. 100 ml

FIG 127 Hyperkalæmia
(a) K+ = 37 mg /100 ml
(b) Recovering as K+ falls

14 m. eq per litre (Fig 126) (2) Shock, dehydration, uræmia, Addison's disease, and diabetic acidosis may lead to a rise in extracellular potassium (Fig. 127)

... QT, largely due to
ncrease in the dura-
me negative (3).

Hypokalæmia may be caused by diabetic acidosis, chronic diarrhœa, or familial periodic paralysis. Prolonged lack of potassium may lead to permanent damage to the heart muscle (4, 5).

Hypercalcæmia The duration of systole is shortened, the QTc time falls to about 0 34 sec. The T wave tends to be small, and to merge with the end of QRS, so that the S-T interval can hardly be seen These rare abnormalities may be met with in hyperparathyroidism (6)

Hypocalcæmia There is increase in the duration of systole so that the Q-T interval is prolonged In some cases the presence of hypopotassæmia alters the T wave, which is otherwise normal. The abnormal points tend to appear when the level of the serum calcium has fallen below 7–8 mg per 100 ml (7) It should be remembered that abnormal electrolytic states are often complex, more than one electrolyte being affected This makes the cardiographic pattern atypical and complicated, so that the diagnosis of any particular condition may be difficult But the degree of cardiographic abnor-

The effect on the cardiogram of coexisting disease must sometimes be allowed for,
times quinidine
heart or myxœde

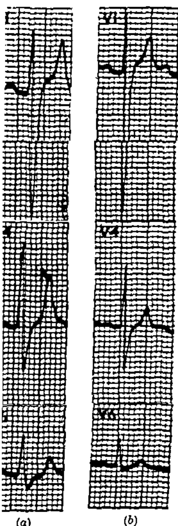
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Failure of the Muscle Cell

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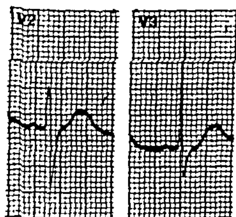


Fig. 128 Hypokalæmia
Serum K^+ 9 mg /100 ml
Normal 14–22 mg /100 ml

Fig. 127 Hyperkalæmia
(a) K^+ = 37 mg /100 ml.
(b) Recovering as K^+ falls

m. eq. per litre (Fig. 126) (2) Shock, dehydration, uræmia, Adon's *disease, and diabetic acidosis may lead to a rise in extra*lular potassium (Fig 127)

Hypokalæmia. There is increased duration of QT, largely due to wed repolarisation (T wave) There may be increase in the duran of the RS-T phase (Fig 128). T may become negative (*3*).

X-rays shows the engorgement of the pulmonary veins and a general lack of translucency while small collections of fluid form in the costodiaphragmatic angles This more often comes when the right ventricle fails ' Clinically the entry of air at the bases of the lungs is poor, there may be a few fine crepitations of œdema. The pulmonary second sound will be accentuated, and equal the aortic second sound in loudness ; When there is hypertension this change

cardiac dyspnœa on very little exertion, or even at rest, or during sleep These may be accompanied by broncho-spasm, or lead to acute pulmonary œdema (p 369) The beat of the left ventricle is increased, as a rule, in area and force, but is actually weak for its size Frequently the thrust is prolonged and actually double, due to the shock of palpable early diastolic filling The heart rhythm usually remains normal with some increase in rate ventricular extrasystoles are not uncommon, the systolic blood pressure tends to fall, except of course in an acute attack. But very varying causes will influence the character of the pulse apart from the vigour of the myocardium

Alternation of the pulse (pulsus alternans). (L. Traube, 1872) A weak beat alternates with a stronger. The spacing is

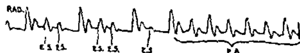


FIG 123 Alternation of the pulse following a bout of extra systoles P A = pulsus alternans

usually regular Occasionally the interval preceding the weaker pulse beat is longer than before the stronger, as the weaker contraction fills the peripheral circulation more slowly The actual cardiac contraction of the weaker beat may be in fact slightly premature (1) Alternation is easily recognised with the sphygmomanometer if the ...

the beat at th... always agree with the pulse Somet...

that the utilisation of substrates is normal. There is defective utilisation of energy. Behind this there may be failure of the production of energy, or of liberation of energy. The fault may be within the contractile proteins (*2*). The actomysin fibril is composed of *polymerised actin and myosin* Depolymerisation is associated with shortening, and so there is contraction and release of energy The polymerised state is stable in the presence of potassium When the "impulse" for activity reaches the cell, the permeability of the cell membrane is increased, the atoms and their electrical charges move as depolarisation takes place Potassium leaves the cell, and the fibrils of actomysin shorten. This is systole. Sodium atoms move in.

In diastole, repolymerisation is done through adenosine triphosphate. In fact this is the source of the systolic energy (*3*). One type of failure where there is disturbance of energy production may be due to lack of oxygen, or some enzyme or hormone, as in myxœdema The other is the derangement in the utilisation of energy. When the heart fails there is a tendency for the electrolytes, potassium and *sodium, to leave the cell, and for water to enter It is clear that this* abnormal distribution of electrolytes may impair the efficiency of contraction. On recovery the excess water leaves the cells and the potassium and sodium are taken in again. The osmolarity of the extra-cellular space may be a very important matter (*4*) Digitalis enables the actinomysin fibril to make better use of the available protein-bound energy and so increase its work without using any more oxygen (*3*).

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Left Ventricular Failure

When the idea became accepted that the left ventricle might fail before the right, an important progressive step was made In the majority of cases of heart disease it was late in the day to think [illegible] appeared. Early diagnosis

[illegible]

infarcts damage mainly the left ventricle. It is here that the default in function first develops in many cases The pulmonary circulation becomes congested and the pressure rises in the pulmonary artery The flow of blood through the lungs slows down The cardiac output remains normal, at the cost of more work Examination with the

more may fail in one part of the muscle than another. Lewis suggested long ago that when the rate of the heart is high, the refractory period of some fibres may last longer than diastole, so that they are not ready to respond to every beat. At slower rates alternation is found in diseased hearts and probably the same defect is responsible Alternation, when it persists, has always been regarded as a sign of the gravest import Few patients live long in whom this serious indication of defective contractility exists for any length of time

Gallop rhythm. (E Potain, 1876.) This is another important sign of ventricular weakness. The name, given by Potain, is hardly a good description, and has caused some confusion, and sometimes the even worse expression "canter rhythm" has been used A third sound is heard. The name "triple rhythm" has also been used. But there is some doubt, if all the varieties of triple rhythm are the same. The phenomenon varies a good deal for two reasons The spacing of the sounds, that is to say the position of the third sound in diastole This variation is related to the rate of the heart, and to the length of diastole The relative loudness of the normal sounds will also alter the cadence the phenomenon sounds different in a hyper-

... in children and young adults, when there is slight nervous acceleration It is generally supposed that the rapid inflow of blood sets up these vibrations Sometimes they can be felt as a slight shock It is rare to find the physiological third sound after middle age ...
with a weak dilated left ve...
logical third sound, but is s...
physiological third sound ...
the auriculo-ventricular valves by the diastolic inflow causes the sound (6) The *presystolic gallop* is associated with auricular systole as Lewis long ago showed (1912) The actual contraction of the auricle can sometimes be heard, particularly if there is heart block There is indeed a loud auricular sound, in view of high diastolic pressure in the ventricle the contraction is more forcible. It has been suggested that the third sound in "gallop" of the presystolic type is the sound of auricular systole transmitted through an atonic ventricular wall (7) When the rate is fast the *early diastolic* and later diastolic sounds may become simultaneous, causing the loud *summation* gallop (8)

T waves (Fig. 130). The finger can rarely detect a difference of less than 20 mm. of mercury, between the beats. It has been shown by the cardiac catheter that alternation may appear in either circulation independently. As one would expect, it is often associated with a raised pressure in either circulation. The variation in the diastolic pressures is always less than the systolic, particularly on the right side. *Electrical alternation* has not been shown in connection with the right ventricle (*2*). Alternation is usually found when the left ventricle is much over-burdened, as in hypertension when failure is threatened It is met with in ischæmic heart disease.

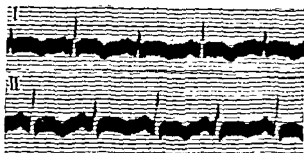


FIG 130. Alternation in voltage of R and T waves

In the tachycardia of flutter, or true paroxysmal tachycardia, alternation may occur, even when the heart is apparently healthy. It disappears when the rate becomes normal It has been detected in fibrillation by sphygmographic records. As heart failure sets in, the alternation may become less obvious It has been suggested that the rising filling pressure may cause an increased stretch of the fibres in diastole and a more uniform beat and more uniform ejection (*3*). But in some cases, while *lowering the venous return* was found to exaggerate the alternation, exercise and intravenous infusion, by raising the venous pressure, had the same effect (*4*, *5*) *Digitalis may* abolish alternation, by improving ventricular contraction This abnormality not uncommonly appears for a short while after extrasystoles (Fig 129) It is important not to mistake bigeminy of the pulse for alternation, a not uncommon error. Here the shorter interval, and it is very obviously shorter as a rule, precedes the weaker beat and exercise may perhaps cause the rhythm to become regular.

THE NATURE OF ALTERNATION. *In alternation all the fibres of* the ventricle do not contract at each systole The fibres that do not respond to the impulse may be diffused throughout the muscle, or

is long-standing pulmonary disease, usually with emphysema, the "chronic cor pulmonale," and the sudden failure due to pulmonary embolism, the "acute cor pulmonale." Primary pulmonary hypertension is a rare cause. Finally there are some of the congenital lesions, pulmonary stenosis, simple or complex, and ventricular and atrial septal defect, also transposition of the great vessels

The signs are those of raised systemic venous pressure, i e engorgement of the jugular veins, enlargement of the liver, œdema and ascites A dull ache under the right ribs denotes the stretching of the liver capsule Incompetence of the tricuspid valve may develop and makes things worse If there is primary right failure the lungs will remain clear. There is no tendency to pulmonary engorgement and œdema, but hydrothorax may develop The enlargement of the right ventricle may be detected by the thrust to the left of the sternum and dullness to the right of it A gallop rhythm is sometimes heard over the right ventricle The pulmonary second sound will be loud, as a rule, unless the valves are deformed

Bernheim's syndrome In some cases of gross concentric hypertrophy of the left ventricle, such as aortic stenosis or hypertension, the greatly thickened sept[illegible]

[illegible] to arise in a case with left side lesions. The lungs are free from congestion and there is no orthopnœa (see p. 185).

Failure of the right ventricle most commonly follows that of the left As it comes on, the acute distress of an over-filled pulmonary circulation is often relieved and the dyspnœa is less intense The acute paroxysms no longer torment The patient feels better but is *really worse* Pregnancy and pulmonary infection, as well as infarction may be causes

Precipitating causes of heart failure. Usually heart failure has a gradual onset with increasing dyspnœa on effort, leading on to orthopnœa, or œdema of the ankles In hypertensive heart disease, nocturnal dyspnœa, with perhaps an attack of acute pulmonary œdema, may betray the presence of advanced pulmonary congestion, with hydrothorax Some acute attacks of pulmonary œdema [illegible]
from [illegible]

There is no doubt about the important part played by the wall of the ventricle, which is weak, atonic and dilated. Further evidence of this is the presence of a slight shock just before the true thrust of systole, or earlier in diastole. This can be seen in thin patients, and often causes the beat to feel double. This vibration goes with the gallop sound

It is noteworthy that "gallop" does not appear with mitral stenosis, and it is most unusual with fibrillation, the one restricting the rate of ventricular filling and the other abolishing auricular systole. If a ventricular beat is dropped the auricular "gallop" sound remains alone. If failure clears, under digitalis particularly, the gallop rhythm disappears.

Clinical significance. Gallop rhythm occurs most commonly in hypertensive heart disease. It is not uncommon after a large left ventricular infarct or any case of ventricular disease as in cardiomyopathy. It is found in severe anæmia. It may be heard over the right ventricle in emphysema and pulmonary infarction It points to failure of the ventricle, and carries a grave prognosis if it persists

DIFFERENTIAL DIAGNOSIS The physiological third sound is probably the same filling phenomenon in a healthy heart The systole of the auricles may sometimes be audible. Asynchronous contraction of the ventricles due to bundle branch block, particularly on the left side may be associated with a widely split first sound and double beat.

"Splitting of the sounds" is quite different to the ear, and should cause no difficulty In the case of the first sound a superficial click follows the actual sound of contraction at the apex At the base splitting of the second sound means asynchronous closure of the semilunar valves. This may be found in healthy hearts, particularly in children. The interval widens on inspiration The pathological association is a change from the normal in the relative pressures, particularly in the pulmonary artery, or in the volume of flow, or in the asynchronous ventricular contraction (bundle branch block) The early diastolic sound, best heard below the pulmonary area, the "opening snap," has a character all its own and can be distinguished by its sharp high-pitched snap or click (9) Its association is with mitral stenosis (p 302)

Right Ventricular Failure

Failure of the left ventricle raises the pressure in the pulmonary artery and so brings about secondary failure of the right. This is much the commonest form. Mitral disease comes next, then there

smaller. The volume of the blood is usually lessened from its abnormally high level, as far as the rather imperfect methods can show (*1*)

Within the heart on the right side the residual pressures in diastole return to normal. Thus the pressure in the right ventricle and right auricle at the end of diastole comes down, and so does that in the femoral vein. In the kidneys there is improvement in the flow of plasma, but even on apparent recovery in other respects, this function may still remain low. But in the first place it would have fallen more than the rate of glomerular filtration, owing to the constriction of the efferent arteriole.

The rate of filtration through the glomeruli returns to normal; as a result there may be four-fold improvement in the excretion of sodium, five-fold in chlorine and two-fold in that of potassium (*1*). The arterial pressure tends to rise, both in systole and diastole. In cases with failure of the left ventricle the pressure in the pulmonary artery falls. If the output goes up, the stroke volume improves, for the rate of the heart will tend to come down. Digitalis is responsible for this improved efficiency, which may be apparent in cases of failure of the right ventricle, where the output may tend to be relatively high (*2*). The pressure in the right ventricle at the end of diastole falls to normal showing that the tendency for residual blood to accumulate is gone.

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Treatment

The digitalis group of drugs. Heart failure is always a call for digitalis. The success of the treatment will depend a good deal on its correct use.

PREPARATIONS. These are obtained from two varieties of foxglove, digitalis purpurea and digitalis lanata (the woolly foxglove) from Austria, with yellow flowers.

Digitalis folium is the dried and powdered leaf of digitalis purpurea, digitalis pulverata or præparata of the British Pharmacopœa [illegible]

preparat [illegible]

[illegible] gram doses (30–60 mg.), a rather ineffective preparation, and not to be confused with the "digitaline crystalise" of Nativelle, which is very much stronger (*1*)

possibility of a painless infarct should be borne in mind in sudden unexpected failure, particularly if there is a previous liability to angina of effort. Ventricular tachycardia causing breakdown may arise in this way.

Rhythm in heart failure. Failure with normal rhythm is the rule in hypertensive heart disease. In heart disease of pulmonary origin a normal rhythm usually persists. The same applies to coronary disease (ischæmic heart disease). It used to be noted in infective endocarditis before treatment was possible. Syphilitic heart disease, less common nowadays, usually kept a normal rhythm. The large number of patients with mitral disease all tended to fibrillate, and so do elderly thyrotoxic patients. The senile type of failure often fibrillates. Fibrillation is the physiological death of the chamber, at any rate for a time, unless quinidine resurrects it, and its end as an effective contractile organ. This does not matter a great deal in the auricles, but the arrhythmia does lower the output, prolong the circulation time, lower the arterial pressure and tend to an insufficient coronary flow. The heart usually increases in size. The vital capacity is diminished. All these points indicate its disadvantages (*10*). Ventricular fibrillation brings immediate loss of consciousness and sudden death as a rule. An increase in extrasystoles in the auricles often heralds fibrillation, and numerous premature beats from different places in the ventricles usually have an ominous significance (p. 314).

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The Hæmodynamics of Recovery

The criteria vary, and are not always very precise. It has not always been convenient to collect the numerous and elaborate pieces of information from very ill patients. On the whole the cardiac output tends to improve, as one might expect, but it is not a specific indication of recovery. More definite is the improvement in the arteriovenous oxygen difference, which fairly constantly becomes

rather faster (8) But for rapid action digoxin does all that is needed by intravenous injection.

Action of digitalis. In 1785 Withering published his account of "the use of the Foxglove," in which he said that it had "a power over the motion of the heart to a degree yet unobserved in any other medicine"

The output of the normal heart may be actually decreased by digitalis, and the heart is diminished in size. There is no rise in the output of urine There is no diuretic effect in health. The enlarged heart which is not in failure does not increase its output when fully under digitalis, it may indeed fall; the pressures in the pulmonary artery and right auricle are not altered (8). It is in failure that the output is increased (9) This is done mainly by increasing the contractile force of the heart beat. Slowing the rate will also help As it is not really understood what goes wrong with the muscle fibres when they fail, so it is not clear what digitalis does to put them right In some way the deficiency in using the chemical energy of adenosine triphosphate is corrected There is no failure to synthesise it, the utilisation of oxygen is normal (4)

Digoxin given into the pulmonary artery caused a rise in the output and in the stroke volume The pressure in the right ventricle at the end of diastole did not alter The pulmonary artery pressure fell The conclusion would be that the left ventricle emptied better (10)

DIURETIC EFFECT Digitalis gained its fame first as a cure for the dropsy The diuretic effect is less striking nowadays with the mercurials to hand Digoxin causes an increase in the excretion of salt and water, at the same time the venous pressure falls The glomerular filtration rate goes up (12) The renal plasma flow increases [illegible] been sugge[illegible] in the ven[illegible] may be some direct action, for injection of digoxin into the renal artery in dogs caused some diuresis (13) There can be no doubt that it is in some way through the improvement of the action of the heart that the diuretic effect is achieved

POTASSIUM AND DIGITALIS If the level of potassium in the serum is low, the level of toxicity of any digitalis preparation will be lower than usual In heart failure there is a tendency for potassium to leave the cells of the myocardium The mercurial diuretics and restriction in diet, the use of resins and d[illegible]

Digitoxin. This is the crystallised digitaline of Nativelle The glycoside is very completely and quickly absorbed, and but slowly excreted Care is needed to avoid a toxic effect. 1·2 mg may be an effective digitalising dose (2). The red granules contain 0·1 mg. (1/600 grain) and the white granules 0·25 mg. (1/240 grain).

Digitalis lanata, contains three crystalline glycosides Lanatoside A, B and C. The leaf of *digitalis lanata* is 3 or 4 times as strong as that of purpurea. On hydrolysis A yields digitoxin, B gives gitoxin, and C, digoxin.

Lanatoside C is marketed as cedilanid in 0·5 mg tablets It acts fast and is quickly excreted (3). The maintenance dose is a tablet a day. It is available in ampoules for intravenous injection.

Digoxin (lanoxin) is the complete glycoside after hydrolysis, which removes glucose and acetic acid This glycoside is rapidly absorbed and rapidly excreted (3). In this country digoxin is used for intravenous injection, 0 5–1·0 mg. The 1 ml ampoule contains 0 5 mg in alcoholic solution It is usually best to give it diluted with saline ten times, but it is quite satisfactory and unlikely to cause local thrombosis if given very slowly, with blood well mixed in the syringe. The tablet of lanoxin contains 0·25 mg. It is pure and constant. The maintenance dose is usually one tablet, but some large patients and large hearts seem to need two daily (4)

Lanoxin (digoxin) is now available for intramuscular or intravenous injection. It is effective and not painful The ampoules of 2 ml. contain 0 5 mg. in 40% propylene glycol and 10% of alcohol.

Gitalin (Gitaligin) is an amorphous water soluble fraction from digitalis purpurea The action is uniform. The therapeutic dose is about half the toxic (5). In most respects it behaves like all other active preparations and is toxic like the rest (6) There are many preparations of digitalis on the market, all should be toxic It is not possible or necessary to know them all, for oral use it is doubtful whether Withering's "beautiful green powder" has been surpassed.

Strophanthin is of little value by mouth because of its erratic rate of absorption (4). For intravenous injection ouabain is a glycoside got from the seeds of strophanthus gratus. Strophanthin K is a mixture of glycosides from strophanthus Kombe Acetyl strophanthin is synthesised from the glucose strophanthidin (8)

Squill has a slight digitalis action, from scillaren A and B is prepared Urginin.

Comparing the rates of action · acetylstrophanthidin is quickest by intravenous injection, with ouabain second, and digoxin and lanatoside C third. Slowest are oral digitoxin and digitalis, with digoxin

(and so in standard II and III). While with the horizontal heart, as in hypertension, they are most obvious in V2 (and so in standard I). The negative T normally seen in VR becomes positive. If the intoxication is severe the QRS complex may be slurred and prolonged It may take from 10 to 14 days, or even 6 weeks sometimes, for the T waves to become normal. Digitalis may interfere with the [illegible] t its use

[illegible] not un-

common in digitalis saturation If there is real poisoning there may be dropped beats, or even complete heart block The effect of digitalis stimulating the vagus may cause some slowing of the sinu-auricular node, and also be responsible for some or most of the A-V block, for atropine will abolish both (Fig. 132)

Premature beats and ventricular tachycardia. Ventricular premature contractions may cause "bigeminy," or "coupling" as it is sometimes called If the rhythm is normal auricular premature [illegible]

[illegible] ventricular tachycardia, usually from the same spot as the isolated beats

The bi-directional type of tachycardia is particularly dangerous; so is the appearance of extrasystoles from many spots Ventricular fibrillation is then a possible consequence. When the heart is poisoned by digitalis its inefficiency is made worse.

Apart from these special myocardial effects loss of appetite comes early, and nausea, and then vomiting Diarrhœa is met with, headache is common, green and yellow vision occasional. Coupling may not be important if it is the sole sign

To relieve intoxication the drug must be left off at once [illegible]

[illegible] and vomiting may have been set up and need glucose to break it

Promezathine (as the HCL or chlorotheophyllinate) known as Phenergan and avomine, have controlled the vomiting sometimes, but careful use of *digitalis* should never lead to these unfortunate episodes

Indications and administration. Congestive heart failure in any form, left or right, is the indication for using digitalis, it must be remembered that the term "congestive failure" usually starts with

action to benefit; 1–2 grammes of the chloride may be given by mouth. It is possible that the notion that relief of œdema mobilises digitalis is false: it is really loss of potassium with the diuresis that enhances the possible toxic effect (*14*).

THE ELECTROCARDIOGRAM AND DIGITALIS. There are three signs of the effect of digitalis on the heart muscle (*8*): those connected with the T wave, showing change in the rate of repolarisation, this

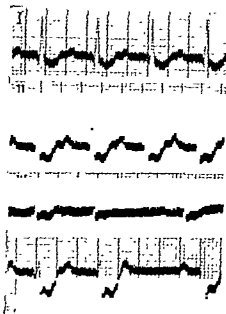


FIG. 131. Digitalis intoxication There is heart block, and depression of S-T interval in all leads, especially IVR.

is a delay, mainly superficial on the surface of the ventricle (*2*), the effect on the auricle-ventricular bundle heart block, (*3*) increase in the excitability of the muscle, premature contractions, and ventricular tachycardia

The T wave First appears depression of the S-T interval This is concave upwards. *The T wave itself is diphasic or inverted* There may be slight shortening of systole. These signs may appear a few hours after intravenous injection The negative T waves must be distinguished if possible from those associated with ventricular hypertrophy (or strain) and those due to ischæmia (Fig 131) The negative T waves may be seen in all limb and chest leads. But with a vertical heart, as in mitral stenosis, they are most obvious in VF

(and so in standard II and III). While with the horizontal heart, as in hypertension, they are most obvious in V2 (and so in standard I) The negative T normally seen in VR becomes positive. If the intoxication is severe the QRS complex may be slurred and prolonged. It may take from 10 to 14 days, or even 6 weeks sometimes, for the T waves to become normal. Digitalis may interfere with the interpretation of electrocardiogram: the information about its use should always be passed on so that allowance can be made.

Heart block. Some prolongation of the P-R interval is not uncommon in digitalis saturation If there is real poisoning there may be dropped beats, or even complete heart block. The effect of digitalis stimulating the vagus may cause some slowing of the sinuauricular node, and also be responsible for some or most of the A-V block, for atropine will abolish both (Fig. 132).

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Promezathine (as the HCL or chlorotheophyll ...

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Indications and administration. Congestive heart failure in any form, left or right, is the indication for using digitalis, it must be remembered that the term "congestive failure" usually starts with

congestion of the pulmonary circulation. The tachycardia of auricular fibrillation and flutter is of course an indication as well (p. 399). As far as heart failure is concerned it does not matter whether the rhythm is normal or whether there is fibrillation. Naturally the quick control of the fast rate is an important step to quick improvement, for the tachycardia may be the main cause of the failure. The

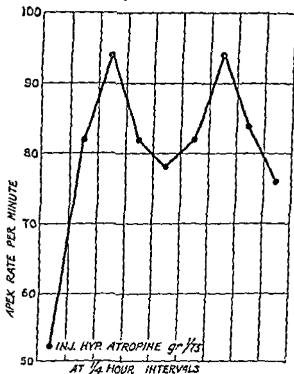


FIG. 132. Chart of apex rate in auricular fibrillation, showing abolition of digitalis slowing by atropine

control of the rate with normal rhythm is less dramatic, but the dyspnœa becomes less, the beat becomes stronger, the systolic pressure may rise, gallop rhythm and alternation disappear, and the signs of pulmonary congestion become less, and œdema clears up with some increase in output of urine This is the characteristic picture of improvement in the failure of the left ventricle burdened by hypertension. Even before signs of failure can be seen, a flagging ventricle will often improve in its work, and carry on better under digitalis, such are the cases of left ventricular enlargement from hypertension and aortic valvular disease

There are some special points for thought

Myocardial infarction. If failure comes on after an infarct it will of course be left ventricular at first The case must be brought under digitalis like any other; the risk of causing ventricular tachycardia is too small to endanger life by withholding the drug (*15*)

Rheumatic carditis. Digitalis is not needed unless there is heart failure It does not act well as a rule

Hyperthyroidism It is almost impossible to control the rate when there is normal rhythm in this condition with digitalis. When there is failure there is usually fibrillation, and for control of this tachycardia very large doses may be needed. But the efficient antithyroid drugs make it easier nowadays (p. 227).

Age For children the dose, as indicated by the weight of the body, is on the same scale as adults These doses are often ineffective in rheumatic carditis, but not because they are too small. On the whole, old people need less than the expected dose, perhaps because the vagus is very sensitive in old age (*3, 16*).

Infections and anæmia Digitalis should not be given in pneumonia unless there is failure With anæmia, myxœdema, beri-beri, arteriovenous aneurysm and Paget's disease, removal of the cause (if possible) is more important than giving digitalis which usually is of little help But this is no contra-indication to its use. There is no point in giving it for angina pectoris

Heart block If the block is complete, digitalis *may be given* if required If the block is partial great care is needed. But by improving the heart's efficiency *the block* may improve Bundle branch block does not matter, it may disappear as the heart improves

Cor pulmonale Just as in hypertension, digitalis is needed to the full, but in these conditions the prospects are sometimes bad, and little success obtainable—unless the infection which has precipitated the f-l-

ligitalis,

...iary, they

y disappear as the heart improves Occasionally auricular tachycardia is abolished by digitalis

Methods Something has been said about some of the many preparations The methods of their use need a little attention

Rapid effect For th...

0 5 mg) 1 0–1 5 mg

mg 0 4 mg Up to 4

Lanoxin can be given by intramuscular injection, 0·5–1·0 mg. Lanatoside C, a glycoside from digitalis, can be given intravenously. It is the same as cedilanid.[*] Nowadays the strophanthus preparations are rarely used; *ouabain* in ampoules of 0·25 mg and strophanthin K (0 25 mg. in 10 ml.) are very quickly active.

Maintaining dosage. To maintain this first effect 2 grains of the leaf may be given by mouth, or 0 25 mg. digoxin (lanoxin) as a tablet. This dose should be repeated every six hours, until the effect is obtained.

Slow effect. This can be obtained by giving the leaf at six-hourly intervals. The loading dose should be about 4 grains for a patient of 10 stone, and thereafter 1 grain six-hourly. The full effect will be achieved in six days If the patient is over 12 stone 1½–2 grains may be given.

Maintenance dose In a patient of average size the maintenance dose is 2–3 grains daily. But patients vary much, and the suitable dose must be found for each one Some may need 4 grains a day. For some it is satisfactory to omit digitalis on one day a week, and so avoid cumulative effect

The pure glycosides are excreted faster than the leaf, and this is usually the best to employ But if it upsets the stomach the Nativelle granules may be tolerated, one red granule (1/600 grain) is about equal to one grain of the leaf.

Despite the large number of preparations on the market all of which no doubt are active, it should suffice to become thoroughly familiar with the powdered leaf, and one of the pure glycosides Then the remark of Wenckebach that a long life hardly sufficed to learn all about this wonderful drug, is less discouraging Perhaps he stressed the word "all."

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Rest and Sleep

The patient must be confined to bed under the care of a competent nurse All unnecessary movements should be avoided, certainly any that cause dyspnœa; and this is the guide when the patient is allowed to attempt them again. A special cardiac bed, of the Lewis

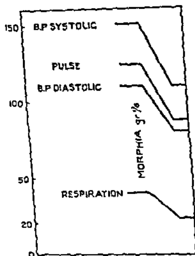


FIG 133 Chart showing the effect of morphia on the pulse, respiration, and blood pressure at the end of half an hour, in an attack of cardiac asthma

type, is useful The arrangement of the pillows is most important, and a suitable bed-rest is very useful Restlessness, anxiety and dyspnœa, with cough, are the chief enemies of sleep The voluntary laboured movements of dyspnœa, which are substituted for the unconscious acts of normal breathing, are disturbing Ventilation may well be diminished if the reflexes working it are quieted

Morphine is the most useful drug in the acute phases of heart failure In the acute attack of left ventricular failure it acts to perfection For the patient who has been sleepless for several nights it may bring the first step of definite improvement The intravenous injection of 1/6 grain (10 0 mg.) is needed ...

suffer after morphine, atropine should be added (1/100 grain: 0 75 mg.). The dose can be repeated for 2 or 3 nights. There is some risk in morphine for the aged; and when there is severe cyanosis as in cor pulmonale, particularly with kyphoscoliosis, but here it is the associated lesions of the lungs that matter.

Other hypnotics If cough is troublesome heroin (1/6 grain : 10 mg.) is useful or physeptone The dry cough of pericarditis or from bronchial irritation by a large left auricle is helped by this, or syrup of codein. A linctus containing heroin (1/6 grain : 10 mg) and codein (1/4 grain : 15 mg.) is useful.

For some patients paraldehyde acts well It can be given in treble doses by the rectum, but may cause irritation, as does intramuscular injection Bromide and chloral are old favourites Nepenthe is useful, also the derivatives of urea, such as carbromal and sedormid. Anxiety and nervousness need the barbiturates. The sodium salts, which most of them are, should be avoided; amytal is as good as any.

Diet

Apart from a low salt diet for use when there is œdema due to retention of sodium, certain principles need attention In severe cases there is often a poor appetite, and there may be nausea and vomiting As a result there may be actual acetonæmia, which calls for glucose, and a low level of proteins in the plasma from too low an intake. Meals increase the work of the heart as the output is increased during digestion Dyspepsia disturbs the heart by leading to ærophagia. Gastric distension or distension of the colon following too much starch, should be avoided In the most acute form of failure, such as after a large infarct, nothing need be given for a day or two but glucose drinks. As soon as possible a light, easily digested, but nutritious diet should be started Meals should be small but evenly spread They are best taken without fluid It is important to tempt the patient's appetite rather than to follow any rigid programme too closely Two schemes of diet are suggested. one light for severe failure, and one a fuller régime for milder cases Starchy food should be reduced if there is flatulence. For cases with coronary disease and high cholesterol level in the blood animal fats should be kept low (butter, cream and fat on meat) (p 238).

Alcohol. Dry sherry and champagne stimulate the appetite Whisky or brandy certainly help some patients, if they like it Small repeated doses may be given. A light dry Rhine wine is often enjoyed.

Vitamins. The acute deficiency of thiamine leads to the wet form of beri-beri This is rare. Minor deficiencies in ascorbic acid and nicotinamide are not uncommon in old people. Orange juice can be added, and nicotinamide given in tablets.

The colon For a few days it is best to leave the bowels alone. Later an enema or suppository can be given After that one of the anthracene group, cascara, aloes, senna or rhubarb combined with a lubricant, is usually effective Salines are best avoided. A commode is better than a bed-pan.

Cardiac cachexia. In advanced cases a cachectic state comes on. No doubt the chronic engorgement of the liver is largely responsible Treatment is now likely to be ineffective Proteins and glucose are the main helps Alcohol is best avoided.

Tobacco Patients with heart failure do best without smoking The inhalation of the smoke causes troublesome coughing The inveterate smoker who finds it hard to give up tobacco is a persistent inhaler as a rule Patients with angina or any tendency to vaso-motor spasm or bad circulation in the legs should *certainly not* smoke But a few cigarettes a day, if the smoke is not inhaled, may prove a comfort to some

AFTER TREATMENT The aim of the after treatment of cardiac failure is to shorten the period of convalescence, and to put the heart in the best state to maintain the circulation as efficiently as may be for as long as possible Rest in bed, with permission to increase the minor activities gradually, should be continued as long as there are any signs of congestion, and until the rate of the heart has been under 80 for a week This is important in cases with normal rhythm

Massage This may help to clear up stubborn œdema It aims at improving the weak and wasted muscles, and stimulating circulation in the legs Thrombosis of veins in the calves may cause

ed unless the calves are

the limb, increasing the

the pulse rate and the respiratory rate are the guides of progress The modern tendency is to avoid chronic invalidism as far as possible and extend

valuable relief, and the hours in bed at night should be long, ten hours or so with advantage. It is the sudden exertion, the short run, that does most harm How much damage buses do by causing persons to run for them!

Prognosis. This is always uncertain, but often much better than might be expected; for a time at any rate Social and economic factors are very important. Failure following fibrillation in mitral disease often does well. Mitral stenosis does better than mitral reflux. Flutter often improves—it here depends on eliminating the fast rate. Cases of right ventricular failure from pulmonary disease do badly as a rule Hypertensive disease may cause failure several times, but each time the prospect gets worse. Congestive failure after myocardial infarction is usually bad, but less so if it comes early and responds to treatment. Much depends on the patient's powers of cooperation. On the whole the obese do badly Usually the larger the heart the worse the outlook Perhaps from the onset of persistent or recurrent œdema one cannot expect much more than two or three years. The hopeful outlook is often more correct than the gloomy; the "Spes cardiaca" must not therefore be damped, each case being judged on its merits Death is usually sudden; but usually not unexpectedly so except in aortic and coronary disease

SYNCOPE

Syncope is the loss of consciousness, or near loss of consciousness, due to acute failure of the circulation The actual cause of unconsciousness may be the sudden loss of support to brain substance from the failure of tension in the arterial tree. acute arterial hypotension is an essential feature (with the possible exception of hypercyanotic syncope in Fallot's tetralogy). Cerebral hypoxia is an important factor when acute hypotension is prolonged

[illegible]

after cardiac arrest induced by ocular compression the first EEG sign is desynchronisation (the response to a painful stimulus), later, slow waves appear which are not necessarily associated with a change in consciousness, but after arrest of more than 14 sec clonic jerks and tonic contraction are accompanied by electrical silence At this stage in epilepsy the cortex is functionally hyper-

active, whereas in a syncopal seizure structures forward of the brain stem are functionally dead (1)

Mechanisms in Syncope

Systemic arterial pressure is a function of cardiac output and total peripheral resistance It follows that acute hypotension may be due primarily to a fall in cardiac output, a failure of the vasomotor system and a fall in peripheral resistance, or to combinations of both

The causes of *cardiogenic syncope* are well known and include: complete heart block (p 293), paroxysmal tachycardia of all types (p 325), extensive cardiac infarction, ball valve thrombus and atrial tumours, massive pulmonary embolism, and cyanotic congenital heart disease (p 293) In Fallot's tetralogy syncope is associated with paroxysmal hypercyanosis and may be due to rapid increase of the right to left shunt caused by spasm of infundibular muscle in the right ventricle (2)

In *vasomotor syncope* (vaso-vagal or better vaso-depressor syncope) many factors interact to cause the faint which is an acute failure of integration in the cardio-vascular system The most important features are a sudden fall of peripheral resistance and loss of cardiac output associated with the upright posture Normal compensation by systemic vasoconstriction is ineffective On the afferent side it is probable that multiple baroceptors are responsive to rapid changes in pulse pressure (3) Normally a decrease in pulse pressure leads to peripheral constriction The general theory of baroceptor responses fits well with observations of vascular reactions accompanying squatting (4), the Valsalva manoeuvre (5), and fast ectopic rhythms where syncope follows if baroceptor constriction does not maintain a systemic arterial pressure of 50 mm Hg or more (6)

The release of normal vasoconstriction with consequent increase of blood flow in the forearm has been shown in the fainting reactions of tilting to an upright position, lordosis, pregnancy and spinal anaesthesia (7) Atropinisation which prevents relative [illegible]

[illegible] the cause of a [illegible] response of cardiac output (8) Predisposing factors to ineffectual vasoconstriction are hot weather, a stuffy atmosphere, general ill health (including convalescence from major illness) and emotional situations confronting a psychoneurotic personality.

POSTURAL HYPOTENSION. Organic disease of the autonomic nervous system either in its central connections or in the periphery, with or without associated neurological disease, may lead to postural hypotension and syncope. A rare form occurs in middle-aged males, and leads to a triad of symptoms: postural syncope, anhydrosis and impotence (*9*). This may be due to a degeneration of autonomic centres in the brain Evidence from a study of three cases pointed to a central failure of the carotid sinus reflex (*10*). Spinal anæsthesia, sympathectomy, or medical sympathectomy with hypotensive drugs, have similar effects, and may lead to postural syncope.

CAROTID SINUS SYNCOPE. Here the fault is on the afferent side and the carotid sinus is abnormally sensitive to pressor stimuli Little has been added to this subject since the condition was described (*11*) but few authorities would now agree with classification into three types (associated with bradycardia, hypotension and cerebral features) as there is a wide range of reaction, and the mechanisms are similar in all Surgical treatment by denervation has been advocated, but in many cases treatment with a long-acting synthetic vagal inhibitor such as oxyphenonium bromide is effective (*12*)

COUGH SYNCOPE was described by Charcot in 1876 as laryngeal vertigo Baker (*13*), having analysed 168 cases from the literature and added 9 new ones, points out that it has nothing to do with the larynx, and vertigo is not a feature Tussive syncope affects men who are plethoric, obese and subject to chronic cough. Attacks are provoked by any stimulus which causes a violent bout of coughing the heart is no more frequently diseased than in "controls." The prognosis is good and relief is assured if coughing can be treated effectively Syncope is probably due to a sudden fall of venous filling pressure with resulting drop in cardiac output followed by acute hypotension

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13. [illegible]

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